

FIGURE 1

AGGCGGGCAGCAGCTGCAGGCTGACCTTGCAGCTTGGCGGAATGGACTGGCCTCACAACTGCTGTTTCTT  
CTTACCATTTCCATCTTCCTGGGGCTGGGCCAGCCCAGGAGCCCCAAAAGCAAGAGGAAGGGGCAAGGGCG  
GCCTGGGCCCCCTGGCCCCCTGGCCCTCACCAGGTGCCACTGGACCTGGTGTACGGATGAAACCGTATGCCC  
GCATGGAGGAGTATGAGAGGAACATCGAGGAGATGGTGGCCCAGCTGAGGAACAGCTCAGAGCTGGCCCAG  
AGAAAGTGTGAGGTCAACTTGCAGCTGTGGATGTCCAACAAGAGGAGCCTGTCCTCCCTGGGGCTACAGCAT  
CAACCACGACCCCAGCCGTATCCCCGTGGACCTGCCGAGGCACGGTGCCTGTGTCTGGGCTGTGTGAACC  
CCTTCACCATGCAGGAGGACCGCAGCATGGTGAGCGTGCCGGTGTTTCAGCCAGGTTCCCTGTGCGCCGCCGC  
CTCTGCCCCGCCACCGCCCCGCACAGGGCCTTGCCGCCAGCGCGCAGTCATGGAGACCATCGCTGTGGGCTG  
CACCTGCATCTTCTGAATCACCTGGCCCAGAAGCCAGGCCAGCAGCCCCGAGACCATCCTCCTTGCACCTTT  
GTGCCAAGAAAGGCCTATGAAAAGTAAACACTGACTTTTGAAAGCAAG

10000157.103001

FIGURE 2

MDWPHNLLFLLTISIFLGLGQPRSPKSKRKGQGRPGPLAPGPHQVPLDLVSRMKPYARMEYERNIEEMVA  
QLRNSSELAQRKCEVNLQLWMSNKRSLSPWGYSINHDPSPRI PVDLPEARCLCLGCVNPFTMQEDRSMVSVF  
VFSQVPVRRRLCPPPPRTGPCRQRAVMETIAVGCTCIF

10000157 "103001

**FIGURE 3**

GCCAGGTGTGCAGGCCGCTCCAAGCCCAGCCTGCCCCGCTGCCGCCACCATGACGCTCCTCCCCGGCCTCC  
TGTTTCTGACCTGGCTGCACACATGCCTGGCCCACCATGACCCCTCCCTCAGGGGGCACCCCCACAGTCAC  
GGTACCCCACTGCTACTCGGCTGAGGAACTGCCCCCTCGGCCAGGCCCCCCCCACACCTGCTGGCTCGAGG  
TGCCAAGTGGGGGCAGGCTTTGCCTGTAGCCCTGGTGTCCAGCCTGGAGGCAGCAAGCCACAGGGGGAGGC  
ACGAGAGGCCCTCAGCTACGACCCAGTGCCCGGTGCTGCGGCCGGAGGAGGTGTTGGAGGCAGACACCCAC  
CAGCGCTCCATCTCACCCCTGGAGATACCGTGTGGACACGGATGAGGACCGCTATCCACAGAAGCTGGCCTT  
CGCCGAGTGCCTGTGCAGAGGCTGTATCGATGCACGGACGGGCCGCGAGACAGCTGCGCTCAACTCCGTGC  
GGCTGCTCCAGAGCCTGCTGGTGTGCGCCGCCGGCCCTGCTCCCGCGACGGCTCGGGGCTCCCCACACCT  
GGGGCCTTTGCCTTCCACACCGAGTTCATCCACGTCCCCGTCGGCTGCACCTGCGTGCTGCCCCGTTCACT  
GTGACCGCCGAGGCCGTGGGGCCCCCTAGACTGGACACGTGTGCTCCCCAGAGGGCACCCCCTATTTATGTG  
TATTTATTGTTATTTATATGCCTCCCCCAACTACCCCTGGGGTCTGGGCATTCCCCGTGTCTGGAGGAC  
AGCCCCCACTGTTCTCCTCATCTCCAGCCTCAGTAGTTGGGGGTAGAAGGAGCTCAGCACCTCTTCCAGC  
CCTTAAAGCTGCAGAAAAGGTGTCACACGGCTGCCTGTACCTTGGCTCCCTGTCCTGCTCCCGGCTTCCCT  
TACCCTATCACTGGCCTCAGGCCCCGCAGGCTGCCTCTTCCCAACCTCCTTGAAGTACCCCTGTTTCTTA  
ACAATTATTTAAGTGTACGTGTATTATTAACTGATGAACACATCCCCAAAA

10000157.103001

FIGURE 5

GGCTTGCTGAAAATAAAATCAGGACTCCTAACCTGCTCCAGTCAGCCTGCTTCCACGAGGCCTGTCAGTCA  
GTGCCCCGACTTGTGACTGAGTGTGCAGTGCCCAGCATGTACCAGGTCAGTGCAGAGGGCTGCCTGAGGGCT  
GTGCTGAGAGGGAGAGGAGCAGAGATGCTGCTGAGGGTGGAGGGAGGCCAAGCTGCCAGGTTTGGGGCTGG  
GGGCCAAGTGGAGTGAGAACTGGGATCCCAGGGGGAGGGTGCAGATGAGGGAGCGACCCAGATTAGGTGA  
GGACAGTTCTCTCATTAGCCTTTTCCTACAGGTGGTTGCATTCTTGGAATGGTCATGGGAACCCACACCT  
ACAGCCACTGGCCCAGCTGCTGCCCCAGCAAAGGGCAGGACACCTCTGAGGAGCTGCTGAGGTGGAGCACT  
GTGCCTGTGCCTCCCCTAGAGCCTGCTAGGCCCAACCGCCACCCAGAGTCCTGTAGGGCCAGTGAAGATGGA  
CCCCTCAACAGCAGGGCCATCTCCCCCTGGAGATATGAGTTGGACAGAGACTTGAACCGGCTCCCCCAGGA  
CCTGTACCACGCCCCGTTGCCTGTGCCCCGCACTGCGTCAGCCTACAGACAGGCTCCCACATGGACCCCCGGG  
GCAACTCGGAGCTGCTCTACCACAACCAGACTGTCTTCTACAGGCGGCCATGCCATGGCGAGAAGGGCACC  
CACAAGGGCTACTGCCTGGAGCGCAGGCTGTACCGTGTTTCCTTAGCTTGTGTGTGTGCGGCCCCGTGT  
GATGGGCTAGCCGGACCTGCTGGAGGCTGGTCCCTTTTTGGGAAACCTGGAGCCAGGTGTACAACCACTTG  
CCATGAAGGGCCAGGATGCCCAGATGCTTGGCCCCTGTGAAGTGCTGTCTGGAGCAGCAGGATCCCGGGAC  
AGGATGGGGGGCTTTGGGAAAACCTGCACTTCTGCACATTTTGAAAAGAGCAGCTGCTGCTTAGGGCCGC  
CGGAAGCTGGTGTCTGTCATTTTCTCTCAGGAAAGGTTTTCAAAGTTCTGCCCATTCTGGAGGCCACCA  
CTCCTGTCTCTTCTCTTTTCCCATCCCCTGCTACCCTGGCCCAGCACAGGCACTTTCTAGATATTTCCCC  
CTTGCTGGAGAAGAAAGAGCCCCTGGTTTTATTTGTTTGTACTCATCACTCAGTGAGCATCTACTTTGG  
GTGCATTCTAGTGTAGTTACTAGTCTTTTGACATGGATGATTCTGAGGAGGAAGCTGTTATTGAATGTATA  
GAGATTTATCCAAATAAATATCTTTATTTAAAAATGAAAAA

10000157.103001



9/70

FIGURE 9

CAACTGCACCTCGGTTCTATCGATAGCCACCAGCGCAACATGACAGTGAAGACCCTGCATGGCCCAGCCAT  
GGTCAAGTACTTGCTGCTGTGATATTGGGGCTTGCCCTTTCTGAGTGAGGCGGCAGCTCGGAAAATCCCCA  
AAGTAGGACATACTTTTTTCCAAAAGCCTGAGAGTTGCCCGCCTGTGCCAGGAGGTAGTATGAAGCTTGAC  
ATTGGCATCATCAATGAAAACCAGCGCGTTTCCATGTCACGTAACATCGAGAGCCGCTCCACCTCCCCCTG  
GAATTACACTGTCACCTGGGACCCCAACCGGTACCCCTCGGAAGTTGTACAGGCCCAGTGTAGGAACTTGG  
GCTGCATCAATGCTCAAGGAAAGGACATCTCCATGAATTCCGTTCCCATCCAGCAAGAGACCCTGGTCGTC  
CGGAGGAAGCACCAAGGCTGCTCTGTTTCTTTCCAGTTGGAGAAGGTGCTGGTGACTGTTGGCTGCACCTG  
CGTCACCCCTGTCATCCACCATGTGCAGTAAGAGGTGCATATCCACTCAGCTGAAGAAG

10000157-103001

10/70

FIGURE 10

MTVKTLHGPMVKYLLLSILGLAFLSEAAARKIPKVGHTFFQKPESCPPVPGGSMKLDIGIINENQRVSMS  
RNIESRSTSPWNYTVTWDPNRYPSEVVQAQCRNLGCINAQGKEDISMNSVPIQQETLVVRRKHQGCSVSFQ  
LEKVLVTVGCTCVTPVIHHVQ

Signal sequence:

Amino acids 1-30

N-glycosylation site:

Amino acids 83-86

N-myristoylation sites:

Amino acids 106-111;136-141

10000157 103001

**FIGURE 11**

CCGGCGATGTCGCTCGTGCTGCTAAGCCTGGCCGCGCTGTGCAGGAGCGCCGTACCCCGAGAGCCGACCGT  
TCAATGTGGCTCTGAAACTGGGCCATCTCCAGAGTGGATGCTACAACATGATCTAATCCCGGAGACTTGA  
GGGACCTCCGAGTAGAACCTGTTACAACAGTGTGCAACAGGGGACTATTCAATTTTGATGAATGTAAGC  
TGGGTACTCCGGGCAGATGCCAGCATCCGCTTGTTGAAGGCCACCAAGATTTGTGTGACGGGCAAAAGCAA  
CTTCCAGTCCTACAGCTGTGTGAGGTGCAATTACACAGAGGCCTTCCAGACTCAGACCAGACCCCTCTGGTG  
GTAAATGGACATTTTCTACATCGGCTTCCCTGTAGAGCTGAACACAGTCTATTTTCATTGGGGCCCATAAT  
ATTCTAATGCAAATATGAATGAAGATGGCCCTTCCATGTCTGTGAATTTACCTCACCAGGCTGCCTAGA  
CCACATAATGAAATATAAAAAAAGTGTGTCAAGGCCGGAAGCCTGTGGGATCCGAACATCACTGCTTGTA  
AGAAGAATGAGGAGACAGTAGAAGTGAAGTTCACAACCACTCCCTGGGAAACAGATACATGGCTCTTATC  
CAACACAGCACTATCATCGGGTTTTCTCAGGTGTTTGAGCCACACCAGAAGAAACAAACGCGAGCTTCAGT  
GGTGATTCCAGTGACTGGGGATAGTGAAGGTGCTACGGTGCAGCTGACTCCATATTTTCTACTTGTGGCA  
GCGACTGCATCCGACATAAAGGAACAGTTGTGCTCTGCCCACAAACAGGCGTCCCTTTCCCTCTGGATAAC  
AACAAAAGCAAGCCGGGAGGCTGGCTGCCTCTCCTCCTGCTGTCTCTGCTGGTGGCCACATGGGTGCTGGT  
GGCAGGGATCTATCTAATGTGGAGGCACGAAAGGATCAAGAAGACTTCCTTTTCTACCACCACACTACTGC  
CCCCATTAAGGTTCTTGTGGTTTACCCATCTGAAATATGTTTCCATCACACAATTTGTTACTTCACTGAA  
TTTCTTCAAAACCATTGCAGAAGTGAAGTTCATCCTTGAAAAGTGGCAGAAAAAGAAAATAGCAGAGATGGG  
TCCAGTGCAAGTGGCTTGCCACTCAAAGAAGGCAGCAGACAAAGTCGTCTTCTTCTTCCAATGACGTCA  
ACAGTGTGTGCGATGGTACCTGTGGCAAGAGCGAGGGCAGTCCAGTGAGAACTCTCAAGACCTCTTCCCC  
CTTGCTTTAACCTTTTCTGCAGTGATCTAAGAAGCCAGATTCTCTGCACAAATACGTGGTGGTCTACTT  
TAGAGAGATTGATACAAAAGACGATTACAATGCTCTCAGTGTCTGCCCCAAGTACCACCTCATGAAGGATG  
CCACTGCTTTCTGTGCAGAACTTCTCCATGTCAAGCAGCAGGTGTCAGCAGGAAAAAGATCACAAGCCTGC  
CACGATGGCTGCTGCTCCTTGTA

10000157.103001

**FIGURE 12**

MSLVLLSLAALCRSAVPREPTVQCGSETGPSPEWMLQHDLPGLRDLRVEPVTTTSVATGDYSILMNVS  
 LRADASIRLLKATKICVTGKSNFQSYSCVRCNYTEAFQTQTRPSGGKWTFYSYIGFPVELNTVYFIGAHNIP  
 NANMNEDGPSMSVNFTSPGCLDHIMYKKKCVKAGSLWDPNITACKKNEETVEVNFTTTPLGNRYMALIQH  
 STIIGFSQVFEHPQKKQTRASVVIPTVDSEGATVQLTPYFPTCGSDCIRHKGTVVLCPTGVPFPLDNNK  
 SKPGGWLPLLLLSLLVATWVLVAGIYLMWRHERIKKTSFSTTTLLPPIKVLVVYPSEICFHHTICYFTEFL  
 QNHCRSEVILEKWQKKKIAEMGPVQWLATQKKAADKVVFLLSNDVNSVCDGTCGKSEGSPSENSQDLFPLA  
 FNLFCSDLRSQIHLHKYVVVYFREIDTKDDYNALSVC PKYHLMKDATAFCAELLHV KQVVSAGKRSQACHD  
 GCCSL

Signal sequence:	Amino acids 1-14
Transmembrane domain:	Amino acids 290-309
N-glycosylation sites:	Amino acids 67-70;103-106;156-159; 183-186;197-200;283-286
cAMP- and cGMP-dependent protein kinase phosphorylation sites:	Amino acids 228-231;319-322
N-myristoylation site:	Amino acids 116-121
Amidation site:	Amino acids 488-491

10000157.103001

**FIGURE 13**

ACACTGGCCAAACAAAAACGAAAGCACTCCGTGCTGGAAGTAGGAGGAGAGTCAGGACTCCCAGGACAGAG  
AGTGACAAACTACCCAGCACAGCCCCCTCCGCCCCCTCTGGAGGCTGAAGAGGGATTCCAGCCCCCTGCCA  
CCCACAGACACGGGCTGACTGGGGTGTCTGCCCCCTTGGGGGGGGCAGCACAGGGCCTCAGGCCTGGGT  
GCCACCTGGCACCTAGAAGATGCTGTGCCCTGGTTCTTGCTGTCTTGGCACTGGGGCCGAAGCCCAGTGG  
TCCTTTCTCTGGAGAGGCTTGTGGGGCCTCAGGACGCTACCCACTGCTCTCCGGGCCTCTCTGCCGCCTC  
TGGGACAGTGACATACTCTGCCTGCCTGGGGACATCGTGCCTGCTCCGGGCCCCGTGCTGGCGCCTACGCA  
CCTGCAGACAGAGCTGGTGCTGAGGTGCCAGAAGGAGACCGACTGTGACCTCTGTCTGCGTGTGGCTGTCC  
ACTTGGCCGTGCATGGGCACTGGGAAGAGCCTGAAGATGAGGAAAAGTTTGGAGGAGCAGCTGACTCAGGG  
GTGGAGGAGCCTAGGAATGCCTCTCTCCAGGCCCAAGTCGTGCTCTCCTTCCAGGCCTACCCTACTGCCCC  
CTGCGTCTGCTGGAGGTGCAAGTGCCTGCTGCCCTTGTGCAGTTTGGTCAGTCTGTGGGCTCTGTGGTATAT  
GACTGCTTCGAGGCTGCCCTAGGGAGTGAGGTACGAATCTGGTCCATACTCAGCCCAGGTACGAGAAGGA  
ACTCAACCACACACAGCAGCTGCCTGCCCTGCCCTGGCTCAACGTGTCAGCAGATGGTGACAACGTGCATC  
TGGTCTGAATGTCTCTGAGGAGCAGCACTTCGGCCTCTCCCTGTACTGGAATCAGGTCCAGGGCCCCCA  
AAACCCCGGTGGCACAACAACTGACTGGACCGCAGATCATTACCTTGAACCACACAGACCTGGTTCCTTG  
CCTCTGTATTACAGGTGTGGCCTCTGGAACCTGACTCCGTTAGGACGAACATCTGCCCCCTCAGGGAGGACC  
CCCGCGCACACCAGAACCTCTGGCAAGCCGCCGACTGCGACTGCTGACCTGCAGAGCTGGCTGCTGGAC  
GCACCGTGCTCGCTGCCCCGAGAAGCGGCACTGTGCTGGCGGGCTCCGGGTGGGGACCCCTGCCAGCCACT  
GGTCCCACCGCTTTCCTGGGAGAACGTCACTGTGGACAAGGTTCTCGAGTTCCCATGTGTAAGGCCACC  
CTAACCTCTGTGTTACAGGTGAACAGCTCGGAGAAGCTGCAGCTGCAGGAGTGCTTGTGGGCTGACTCCCTG  
GGGCCTCTCAAAGACGATGTGCTACTGTTGGAGACACGAGGCCCCCAGGACAACAGATCCCTCTGTGCCTT  
GGAACCCAGTGGCTGTACTTCACTACCCAGCAAAAGCCTCCACGAGGGCAGCTCGCCTTGGAGAGTACTTAC  
TACAAGACCTGCAGTCAGGCCAGTGTCTGCAGCTATGGGACGATGACTTGGGAGCGCTATGGGCCTGCCCC  
ATGGACAAATACATCCACAAGCGCTGGGCCCTCGTGTGGCTGGCCTGCCTACTCTTTGCCGCTGCGCTTTC  
CCTCATCCTCCTTCTCAAAAAGGATCACGCGAAAGGGTGGCTGAGGCTCTTGAAACAGGACGTCCGCTCGG  
GGGCGGCCCGCAGGGGGCCGCGGGCTCTGCTCCTTACTCAGCCGATGACTCGGGTTTCGAGCGCCTGGTG  
GGCGCCCTGGCGTCGGCCCTGTGCCAGCTGCCGCTGCGCGTGGCCGTAGACCTGTGGAGCCGTCGTGAAC  
GAGCGCGCAGGGGGCCGCTGGTTTACGCGCAGCGCGCCAGACCCTGCAGGAGGGCGGCGTGGTG  
TCTTGCTCTTCTCTCCCGGTGCGGTGGCGCTGTGCAGCGAGTGGCTACAGGATGGGGTGTCCGGGCCCCGG  
GCGCACGGCCCGCACGACGCTTCCGCGCCTCGCTCAGCTGCGTGCTGCCCCACTTCTTGAGGGCCGGGC  
GCCCCGACGCTACGTGGGGGCTGCTTCGACAGGCTGCTCCACCCGACGCCGTACCCGCCCTTTTCCGCA  
CCGTGCCCGTCTTCACTGCCCCCTCCAACTGCCAGACTTCTTGGGGGCCCTGCAGCAGCCTCGCGCCCCG  
CGTTCGGGGCGGCTCCAAGAGAGAGCGGAGCAAGTGTCCCGGGCCCTTACGCCAGCCCTGGATAGCTACTT  
CCATCCCCCGGGGACTCCCGCGCCGGGACGCGGGGTGGGACCAGGGGCGGGACCTGGGGCGGGGGACGGGA  
CTTAAATAAAGGCAGACGCTGTTTTTCTAAAAAA

10000157.103001

**FIGURE 14**

MPVPWFLLSLALGRSPVVLSELERLVGPQDATHCSPGLSCRLWSDILCLPGDIVPAPGPVLAPTHLQTELV  
LRCQKETDCDLCLRVAVHLAVHGHWEPEDEEKFGGAADSGVEEPRNASLQAQVVLSFQAYPTARCVLLEV  
QVPAALVQFGQSVGSVVYDCFEAALGSEVRIWSYTQPRYEKELNHTQQLPALPWLNV SADGDNVHLVLNV  
EEQHFGLSLYWNQVQGPPKPRWHKNLTGPQIITLNHTDLVPCLCIQVWPLEPDSVRTNICPFREDPRAHQ  
LWQAARLRLTLQSWLLDAPCSLPAEAALCWRAPGGDPCQPLVPPLSWENVTVDKVLEFPLLKGHPNLCVQ  
VNSSEKLQEQECLWADSLGPLKDDVLLLETRGPQDNRSLEPSGCTSLPSKASTRAARLGEYLLQDLQS  
GQCLQLWDDDLGALWACPMCKYIHKRWALVWLACLLFAAALSLLLLKKDHAKGWLRLKQDVRSGAAARG  
RAALLLYSADDSGFERLVGALASALCQLPLRVAVDLWSRRELSAQGPVAFHQAQRQTLEGGVVVLLFSP  
GAVALCSEWLQDGVSGPGAHGPHDAFRASLSCVLPDFLQGRAPGSYVGACFDRLHPDAVPALFRTVPVFT  
LPSQLPDFLGALQQPRAPRSGRQLQERAEQVSRAALQPALDSYFHPPGTPAPGRGVGPGAGPGAGDGT

signal sequence:

Amino acids 1-20

transmembrane domain:

Amino acids 453-473

N-glycosylation sites:

Amino acids 118-121;186-189;198-201;  
211-214;238-241;248-251;334-337;  
357-360;391-394

Glycosaminoglycan attachment site: Amino acids 583-586

cAMP- and cGMP-dependent protein kinase phosphorylation site:

Amino acids 552-555

N-myristoylation sites:

Amino acids 107-112;152-157;319-324;  
438-443;516-521;612-617;692-697;  
696-701;700-705

1000157.10001

FIGURE 16

MGSSRLAALLPLLLIVIDLSDSAGIGFRHLPHWNTRCPLASHTDDSFSGSSAYIPCRTWWALFSTKPWCV  
RVWHCSRCLCQHLLSGGSLQRGLFHLLVQSKKSSTFKFYRRHKMPAPAQRKLLPRRHLSEKSHHISIPS  
PDISHKGLRSKRTQPSDPETWESLPRLDSQRHGGPEFSFDLLPEARAIRVTISSGPEVSVRLCHQWALECE  
ELSSPYDVQKIVSGGHTVELPYEFLLPCLCIEASYLQEDTVRRKKCPFQSWPEAYGSDFWKSVHFTDYSQH  
TQMVMAITLRCPLKLEAALCQRHDWHTLCKDLPNATARESDGWYVLEKVDLHPQLCFKFSFGNSSHVECPH  
QTGSLTSWNVSMDTQAQQLILHFSSRMHATFSAAWSLPGLGQDTLVPPVYTVSQARGSSPVSLDLIIPFLR  
PGCCVLVWRSDVQFAWKHLLCPDVSYRHLGLLILALLALLTLLGVVLALTLCRRPQSGPGPARPVLLLHAAD  
SEAQRRLVGALAEALLRAALGGGRDVIVDLWEGRHVARVGPLPWLWAARTRVAREQGTVLLLWSGADLRPVS  
GPDPRAPLLALLHAAPRPLLLLAYFSRLCAKGDIPPLRALPRYRLRLDLPRLLRALDARPF AEATSWGR  
LGARQRRQSRLELC SRLERE AARLADLG

Signal peptide: Amino acids 1-23

Transmembrane domain: Amino acids 455-472

N-glycosylation sites: Amino acids 318-322;347-351;364-368

---

Glycosaminoglycan attachment site: Amino acids 482-486

cAMP- and cGMP-dependent protein kinase phosphorylation sites:  
Amino acids 104-108;645-649

Tyrosine kinase phosphorylation site: Amino acids 322-329

N-myristoylation sites: Amino acids 90-96;358-364;470-476

Eukaryotic cobalamin-binding proteins: Amino acids 453-462

10000157-103001

**FIGURE 17**

GCCAGGCCCTATCTCCCTGCCAGGAGGCCGGAGTGGGGGAGGTGAGACGGGGCGGTTGGAGGGGGAGGGAT  
GCCACGCGCTTCTGCCTCAGGTGTTCTGCGTTGTTTGTGTCAGTGGAGAGCAGGGAGTGGGGCCAGCCAGCA  
GAAACAGTGGGCTGTACAACATCACCTTCAAATATGACAATTGTACCACCTACTTGAATCCAGTGGGGAAG  
CATGTGATTGCTGACGCCCAGAATATCACCATCAGCCAGTATGCTTGCCATGACCAAGTGGCAGTCACCAT  
TCTTTGGTCCCCAGGGGCCCTCGGCATCGAATTCCTGAAAGGATTTTCGGGTAATACTGGAGGAGCTGAAGT  
CGGAGGGAAGACAGTGCCAACTGATTCTAAAGGATCCGAAGCAGCTCAACAGTAGCTTCAAAGAAGT  
GGAATGGAATCTCAACCTTTCCTGAATATGAAATTTGAAACGGATTATTTTCGTAAAGGTTGTCCCTTTTCC  
TTCCATTAAAAACGAAAGCAATTACCACCCTTCTTCTTTAGAACCCGAGCCTGTGACCTGTTGTTACAGC  
CGGACAATCTAGCTTGTAAACCCTTCTGGAAGCCTCGGAACCTGAACATCAGCCAGCATGGCTCGGACATGC  
AGGTGTCCTTCGACCACGCACCCGCATGGCTCGGACATGCAGGTGTCCTTCGACCACGCACCCGCACAACTTC  
GGCTTCCGTTTCTTCTATCTTCACTACAAGCTCAAGCACGAAGGACCTTTCAGCGAAAGACCTGTAAGCA  
GGAGCAAACCTACAGAGATGACCAGCTGCCTCCTTCAAATGTTTCTCCAGGGGATTATATAATTGAGCTGG  
TGGATGACACTAACACAACAAGAAAAGTGATGCATTATGCCTTAAAGCCAGTGCCTCCCCGTGGGCCGGG  
CCCATCAGAGCCGTGGCCATCACAGTGCCACTGGTAGTCATATCGGCATTTCGCGACGCTCTTCACTGTGAT  
GTGCCGCAAGAAGCAACAAGAAAATATATATTACATTTAGATGAAGAGAGCTCTGAGTCTTCCACATACA  
CTGCAGCACTCCCAAGAGAGAGGCTCCGGCCGCGGCCGAAGGTCTTCTCTGCTATTCCAGTAAAGATGGC  
CAGAATCACATGAATGTGTCAGTGTTTCGCCTACTTCCTCCAGGACTTCTGTGGCTGTGAGGTGGCTCT  
GGACCTGTGGGAAGACTTCAGCCTCTGTAGAGAAGGGCAGAGAGAATGGGTCAATCCAGAAGATCCACGAGT  
CCCAGTTCATCATTGTGGTTTGTTCCAAAGGTATGAAGTACTTTGTGGACAAGAAGAACTACAAACACAAA  
GGAGGTGGCCGAGGCTCGGGGAAAGGAGAGCTCTTCTGTTGGCGGTGTCAGCCATTGCCGAAAAGCTCCG  
CCAGGCCAAGCAGAGTTTCGTCCGCGGCGCTCAGCAAGTTTATCGCCGTCTACTTTGATTATTCCTGCGAGG  
GAGACGTCCCCGGTATCCTAGACCTGAGTACCAAGTACAGACTCATGGACAATCTTCTCAGCTCTGTTCC  
CACCTGCACTCCCGAGACCACGGCCTCCAGGAGCCGGGGCAGCACACGCGACAGGGCAGCAGAAGGAACTA  
CTTCCGGAGCAAGTCAGGCCGGTCCCTATACGTCGCCATTTGCAACATGCACCAAGTTTATTGACGAGGAGC  
CCGACTGGTTTCGAAAAGCAGTTTCGTTCCCTTCCATCCTCCTCCACTGCGCTACCGGGAGCCAGTCTTGAG  
AAATTTGATTTCGGGCTTGGTTTTAAATGATGTCATGTGCAAACCAGGGCCTGAGAGTGAATCTGCCTAAA  
GGTAGAGGCGGCTGTTCTTGGGGCAACCGGACCAGCCGACTCCCAGCACGAGAGTCAGCATGGGGGCCTGG  
ACCAAGACGGGGAGGCCCGGCCTGCCCTTGACGGTAGCGCCGCCCTGCAACCCCTGCTGCACACGGTGAAA  
GCCGGCAGCCCCTCGGACATGCCGCGGGACTCAGGCATCTATGACTCGTCTGTGCCCTCATCCGAGCTGTC  
TCTGCCACTGATGGAAGGACTCTCGACGGACCAGACAGAAACGTCTTCCCTGACGGAGAGCGTGTCTCCT  
CTTCAGGCCTGGGTGAGGAGGAACCTCCTGCCCTTCTTCCAAGCTCCTCTCTTCTGGGTGATGCAAAGCA  
GATCTTGGTTGCCGAGCTACACTGATGAATCCACGCGGTGCCCCCTTTGTAACAAAACGAAAGAGTCTA  
AGCATTGCCACTTTAAAAA

1000157-103001



**FIGURE 15**

CGAGGGCTCCTGCTGGTACTGTGTTGCTGCTGCACAGCAAGGCCCTGCCACCCACCTTCAGGCCATGCAG  
CCATGTTCCGGGAGCCCTAATTGCACAGAAGCCCATGGGGAGCTCCAGACTGGCAGCCCTGCTCCTGCCTC  
TCCTCCTCATAGTCATCGACCTCTCTGACTCTGCTGGGATTGGCTTTCGCCACCTGCCCCACTGGAACACC  
CGCTGTCCTCTGGCCTCCCACACGGATGACAGTTTCACTGGAAGTTCTGCCTATATCCCTTGCCGCACCTG  
GTGGGCCCTCTTCTCCACAAAGCCTTGGTGTGTGCGAGTCTGGCACTGTTCCCGCTGTTTGTGCCAGCATCTGC  
TGTCAGGTGGCTCAGGTCTTCAACGGGGCCTCTTCCACCTCCTGGTGCAGAAATCCAAAAAGTCTTCCACA  
TTCAAGTTCTATAGGAGACACAAGATGCCAGCACCTGCTCAGAGGAAGCTGCTGCCTCGTCGTCACCTGTC  
TGAGAAGAGCCATCACATTTCCATCCCCTCCCCAGACATCTCCACAAAGGGACTTCGCTCTAAAAGGACCC  
AACCTTCGGATCCAGAGACATGGGAAAGTCTTCCCAGATTGGACTCACAAAGGCATGGAGGACCCGAGTTC  
TCCTTTGATTTGCTGCCTGAGGCCCGGGCTATTGCGGTGACCATATCTTCAGGCCCTGAGGTCAGCGTGCG  
TCTTTGTCACCACTGGGCACTGGAGTGTGAAGAGCTGAGCAGTCCCTATGATGTCCAGAAAATTGTGTCTG  
GGGGCCACACTGTAGAGCTGCCTTATGAATTCCTTCTGCCCTGTCTGTGCATAGAGGCATCCTACCTGCAA  
GAGGACACTGTGAGGCGCAAAAATGTCCCTTCAGAGCTGGCCAGAAGCCTATGGCTCGGACTTCTGGAA  
GTCAGTGCACCTTCACTGACTACAGCCAGCACACTCAGATGGTCATGGCCCTGACACTCCGCTGCCCACTGA  
AGCTGGAAGCTGCCCTCTGCCAGAGGCACGACTGGCATACCCTTTGCAAAGACCTCCCGAATGCCACGGCT  
CGAGAGTCAGATGGGTGGTATGTTTTGGAGAAGGTGGACCTGCACCCCCAGCTCTGCTTCAAGTTCTCTTT  
TGAAACAGCAGCCATGTTGAATGCCCCCACCAGACTGGGTCTCTCACATCCTGGAATGTAAGCATGGATA  
CCCAAGCCCAGCAGCTGATTCTTCACTTCTCCTCAAGAATGCATGCCACCTTCAGTGCTGCCTGGAGCCTC  
CCAGGCTTGGGGCAGGACACTTTGGTGCCCCCGTGTACACTGTCAGCCAGGCCCGGGGCTCAAGCCCAGT  
GTCACTAGACCTCATCATTTCCCTTCCCTGAGGCCAGGGTGCTGTGTCTGCTGGTGTGGCGGTGAGATGTCCAGT  
TTGCCTGGAAGCACCTCTTGTGTCCAGATGTCTCTTACAGACACCTGGGGCTCTTGATCCTGGCACTGCTG  
GCCCTCCTCACCCCTACTGGGTGTTGTTCTGGCCCTCACCTGCCGGCGCCACAGTCAGGCCCGGGCCAGC  
GCGGCCAGTGCTCCTCCTGCACGCGGCGGACTCGGAGGCGCAGCGCGCCTGGTGGGAGCGCTGGCTGAAC  
TGCTACGGGCAGCGCTGGGCGGCGGGCGGACGTGATCGTGACCTGTGGGAGGGGAGGCACGTGGCGCGCGT  
'GGGCCCCGCTGCCGTGGCTCTGGGCGGCGGGACGCGCGTAGCGGGAGCAGGGCACTGTGCTGCTGCTGT  
GGAGCGGCGCCGACCTTCGCCCCGTGACGGCCCCGACCCCCGCGCGCGCCCCCTGCTCGCCCTGCTCCAC  
GCTGCCCCGCGCCCGCTGCTGCTGCTCGCTTACTTCAGTCGCTCTGCGCCAAGGGCGACATCCCCCGCC  
GCTGCGCGCCCTGCCGCGCTACCGCCTGCTGCGCGACCTGCCGCGTCTGCTGCGGGCGCTGGACGCGCGGC  
CTTTCGAGAGGCCACCAGCTGGGGCCGCTTGGGGCGCGGCAGCGCAGGCAGAGCCGCTAGAGCTGTGC  
AGCCGGCTTGAACGAGAGGCCGCCGACTTGACAGCTAGGTTGAGCAGAGCTCCACCGCAGTCCCCGGGTGTCT

10000157 - 103001

**FIGURE 18**

MPRASASGVPALFVSQGVGPASRNSGLYNITFKYDNCTTYLNPVGKHVIADAQNITISQYACHDQVAVT  
 ILWSPGALGIEFLKGFRVILEELKSEGRQCQQLILKDPKQLNSSFKRTGMESQPFLLMKFETDYFVKVVPF  
 PSIKNESNYHPFFFRTRACDLLLQPDNLACKPFWKPRNLNISQHGSDMQVSFDHAPHGSDMQVSFDHAPHN  
 FGFRFFYLHYKLKHEGPFKRKTCKQEQTTEMTSCLLQNVSPGDYIIELVDDTNTTRKVMHYALKPVHSPWA  
 GPIRAVAITVPLVVISAFATLFTVMCRKKQQENIYSHLDEESSESSTYTAALPRERLRPRPKVFLCYSSKD  
 GQNHMNVVQCFAYFLQDFCGCEVALDLWEDFSLCREGQREWVIQKIHESQFIIIVVCSKGMKYFVDKKNYKH  
 KGGGRGSGKGELFLVAVSAIAEKLQAKQSSSAALSKFIAVYFDYSCEGDVPGILDSTKYRLMDNLPQLC  
 SHLHSRDHGLQEPGQHTRQGSRRNYFRSKSGRSLYVAICNMHQFIDEEPWFEEKQFVFPFHPPLRYREPVL  
 EKFDGLVNDVMCKPGPESDFCLKVEAAVLGATGPADSQHESQHGGLDQDGEARPALDGSAALQPLLHTV  
 KAGSPSDMPRDSGIYDSSVPSSELSLPLMEGLSTDQTETSSLTESVSSSSGLGEEEPALPSKLLSSGSK  
 ADLGCRSYTDELHAVAPL

Transmembrane domain:

Amino acids 283-307

N-glycosylation sites:

Amino acids 31-34;38-41;56-59;  
 113-116;147-150;182-185;266-269

~~Glycosaminoglycan attachment sites: Amino acids 433-436;689-692~~

cAMP- and cGMP-dependent protein kinase phosphorylation:

Amino acids 232-235

Tyrosine kinase phosphorylation sites:

Amino acids 312-319;416-424

N-myristoylation site:

Amino acids 19-24;375-380;428-433;  
 429-434;432-437;517-522;574-579;  
 652-657;707-712

10000157 103001

FIGURE 19

h-IL17 1 ..... MTPGKTSLSVSL L L L S L E A I V K A G I T I P R  
h-IL17B 1 ..... MDWPHNLLFLLTISIFLGLGOPRSPKSKRKGOGR P G P L A P G P  
h-IL17C 1 M T L L P G L L F L T W L H T C L A H H D P S L R G H P H S H G T P H C Y S A E E L P L G Q A P P H  
h-IL17D 1 ..... M L V A G F L L A L P P S W A A G A P R A G R R P A R P R G C A D R P  
h-IL17E 1 ..... M R E R P R L G E D S S L I S L F L O V V A F L A M V M G T H T Y S H  
h-IL17F 1 ..... M T V K T L H G P A M V K Y L L S I L G L A F L S E A A R K I P K V G

h-IL17 30 N P G C P N S E D K N F P R T V M V N L N I H N R N T N T N P K ..... R S S D  
h-IL17B 43 H Q V P L D L V S R M K P Y A R M E E Y E R N I E E M V A O L R N S S E L A O R K C E V N L Q L W M  
h-IL17C 51 L L A R G A K W G O A L P V A L V S S L E A A S H R G R H E R P S A T T O C P V L R P E E V L E A D  
h-IL17D 36 E E L L E Q L Y G R L A A G V L S A F H H T L Q L G P R E O A R N N A S C P A G G R P A D R R F R P P  
h-IL17E 36 W P S C C P S K G O D T S E E L L R W S T V P V P P L E P A R P N R H P E S C R A S ..... E D G P  
h-IL17F 38 H T F F Q K P E S C P P V P G G S M K L D I G I I N E N O R V S ..... M S R N

h-IL17 66 Y Y N R S T S P W N L H R N E D P E R Y P S V I W E A K C R H L G C I N A D G N V O Y H M N S V P  
h-IL17B 93 S N K R S L S P W G Y S I N H O P S R I P V D L P E A R C L C L G C V N P F T M Q E D R S M V S V P  
h-IL17C 101 T H O R S I S P W R Y R V D T D E D R Y P O K L A F A E C L C R G C I D A R T G R E T A A L N S V R  
h-IL17D 86 T N L R S V S P W A Y R I S Y D P A R Y P R Y L P E A Y C L C R G C L T G L F G E E D V R F R S A P  
h-IL17E 82 L N S R A I S P W R Y E L D R L N R L P O D L Y H A R C L C P H C V S L O T G S H M O P R G N S E  
h-IL17F 74 I E S R S T S P W N Y T V T W D P N R Y P S E V V O A O C R N L G C I N A O G K E D I S M N S V P

h-IL17 135 I O Q E I L V L R R E ..... P P H C P N S F R L E K I L Y S V G C T C V T P I V H H V A  
h-IL17B 143 V F S O V P V R R R L C P P P ..... P R T G P C R O R A Y M E T I A V G C T C I F .....  
h-IL17C 151 L L O S L L V L R R R P C S R D G S G L P T P G A F A F H T E F I H V P V G C T C V L P R S V .....  
h-IL17D 136 V Y M P T V L V L R R T P A C A G ..... G R S V Y T E A Y V T I P V G C T C V P E P E K D A D  
h-IL17E 132 L L Y H N O T V F Y R R P C H G E K ..... G T H K G Y C L E R R L Y R V S L A C V C V R P R V M G .....  
h-IL17F 123 I O Q E T L V V R R K ..... H O G C S V S F O L E K V L V T V G C T C V T P V I H H V O

h-IL17D 179 S I N S S I O K O G A K L L L G P N D A P A G P X

10000157-103001

FIGURE 20

10000157 103001

IL17B distribution

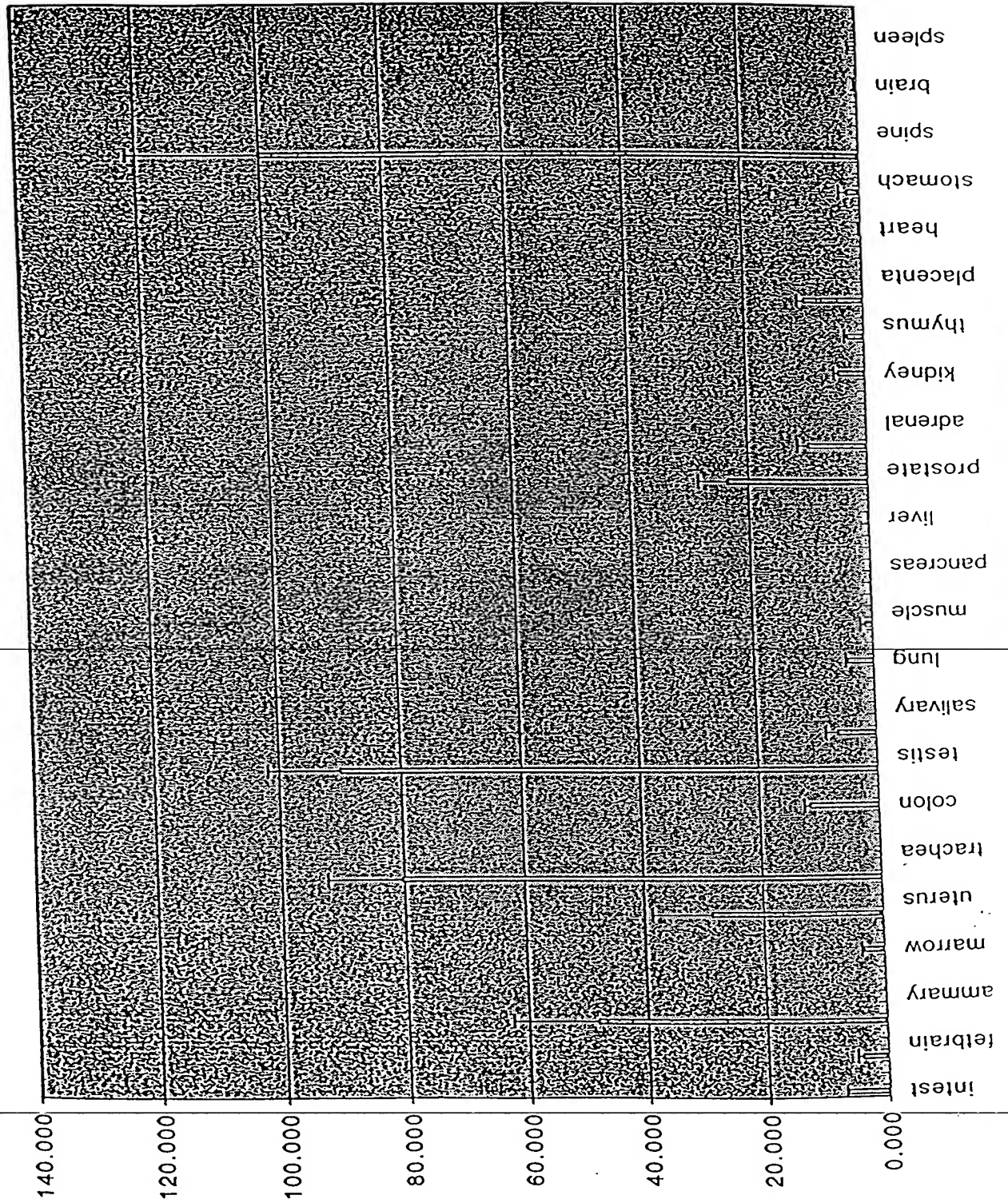
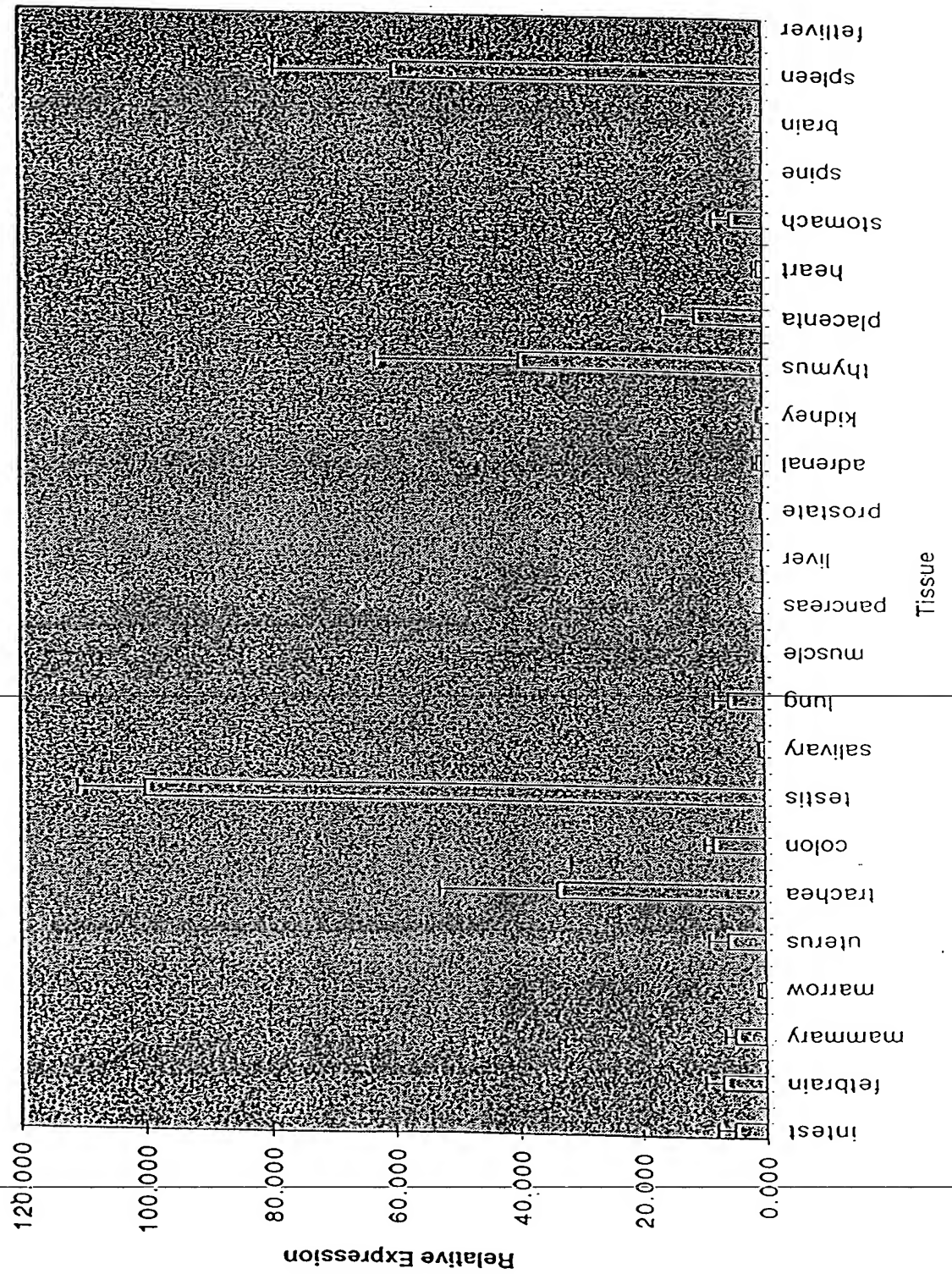


FIGURE 21

## IL17C Distribution



T00E0T" 25T0000T



## IL17D Distribution

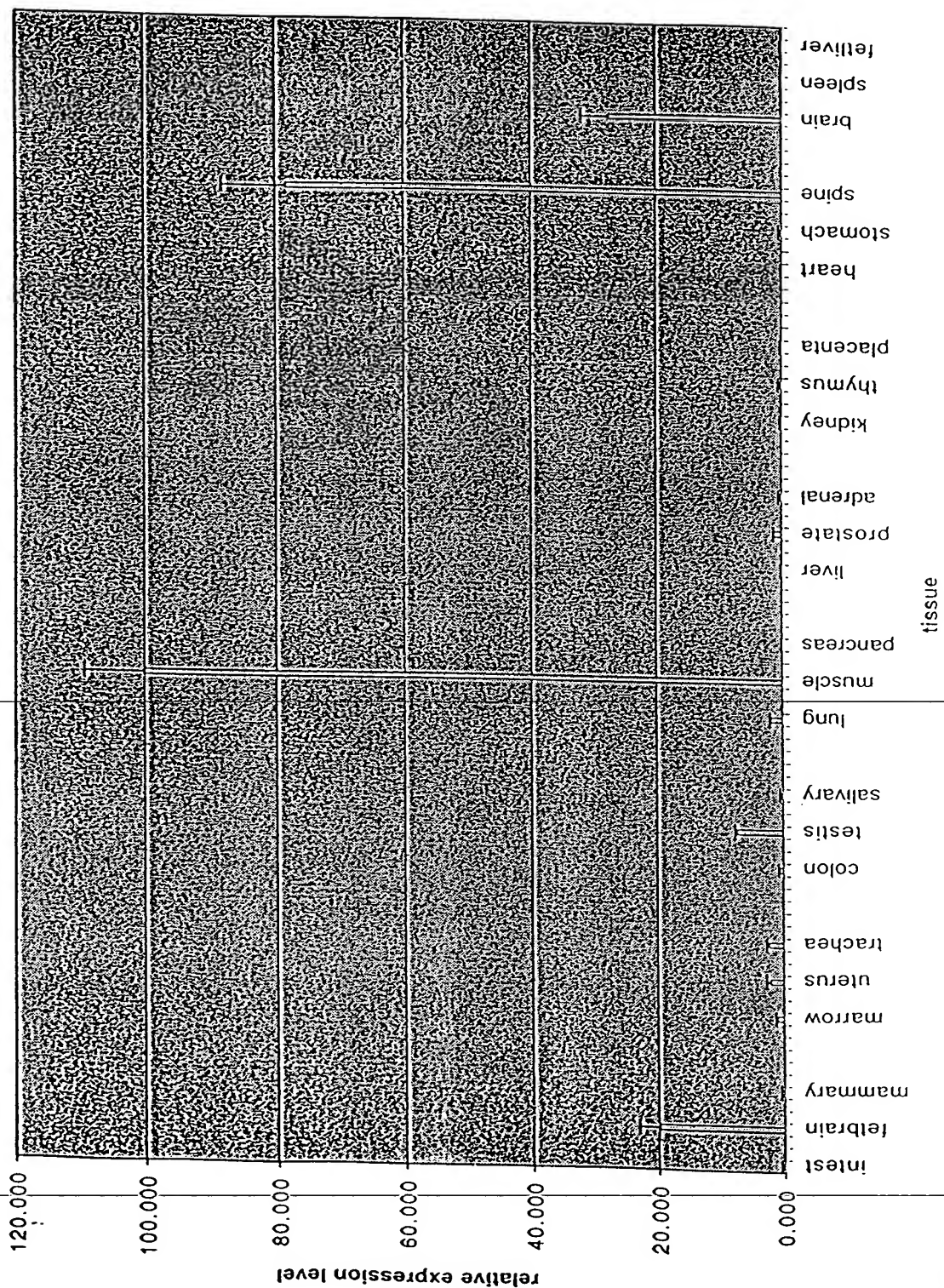


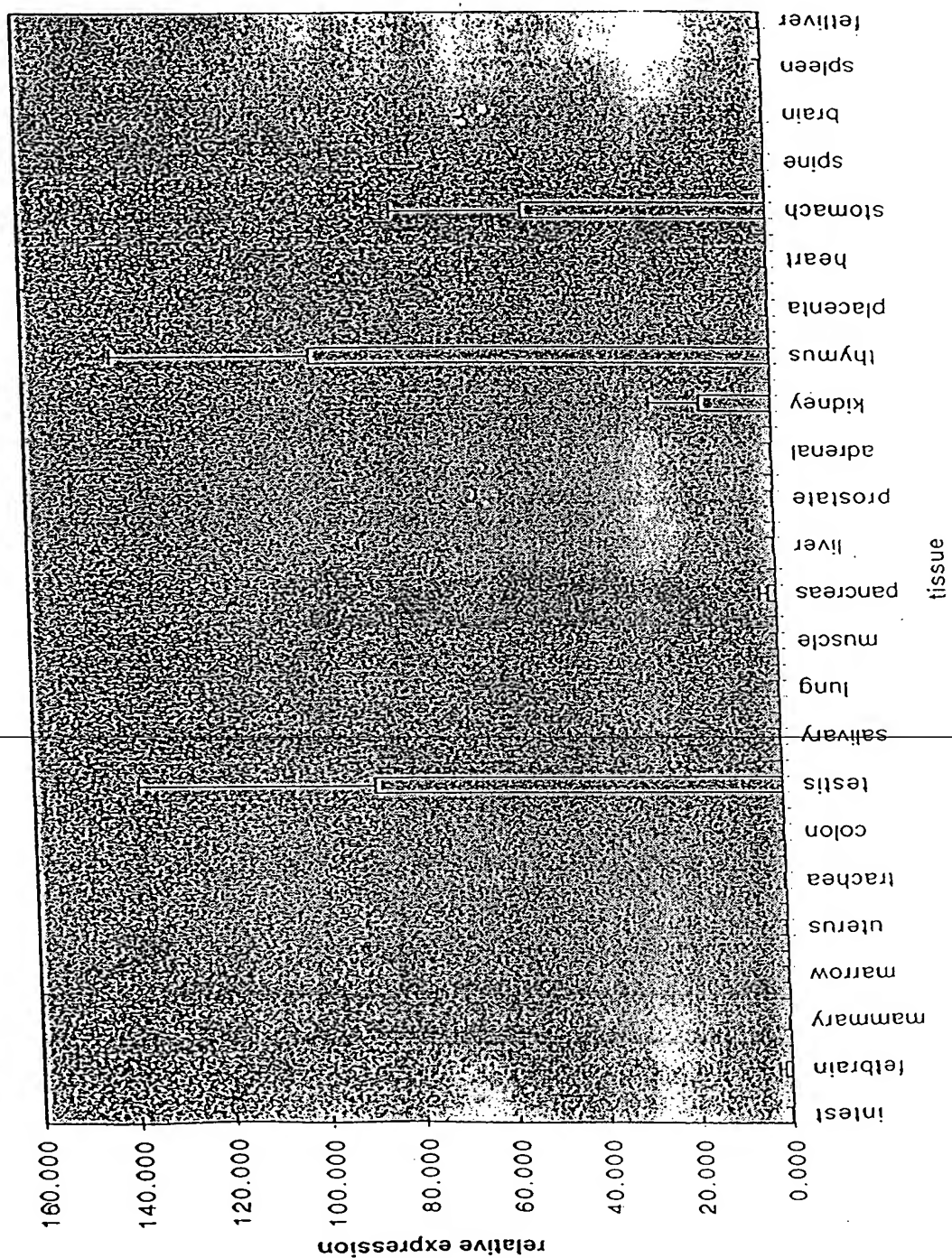
FIGURE 23

Brain	
heart	
kidney	
liver	
lung	
colon	
marrow	
intestine	
spleen	
stomach	
thymus	
prostate	
muscle	
testis	
uterus	
fetal brain	
fetal liver	
spinal chord	
placenta	
adrenal	
pancreas	
salivary	
trachea	
mammary	

FOOTNOTES

FIGURE 24

## IL17 F Distribution

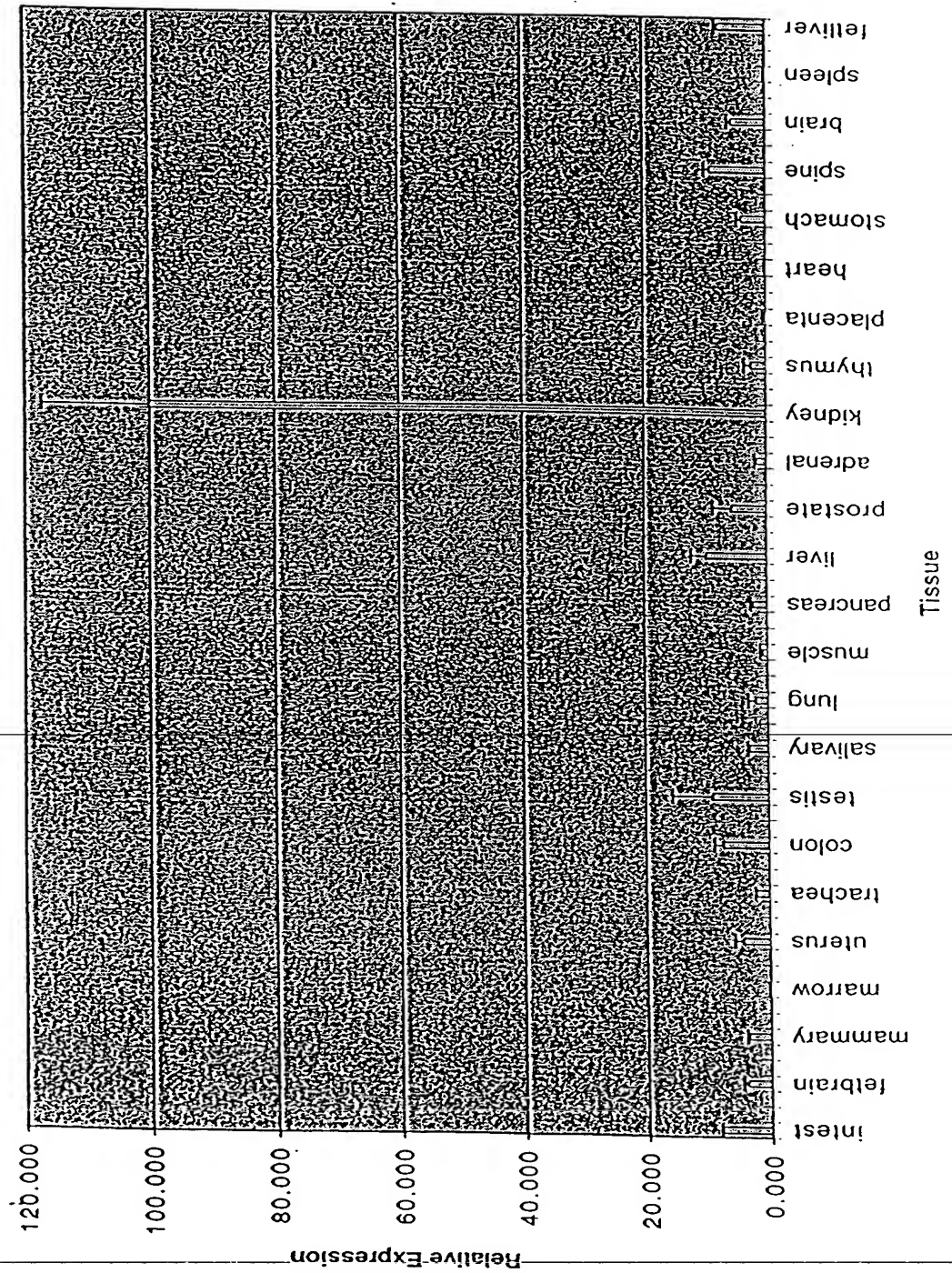


100000157 1030001



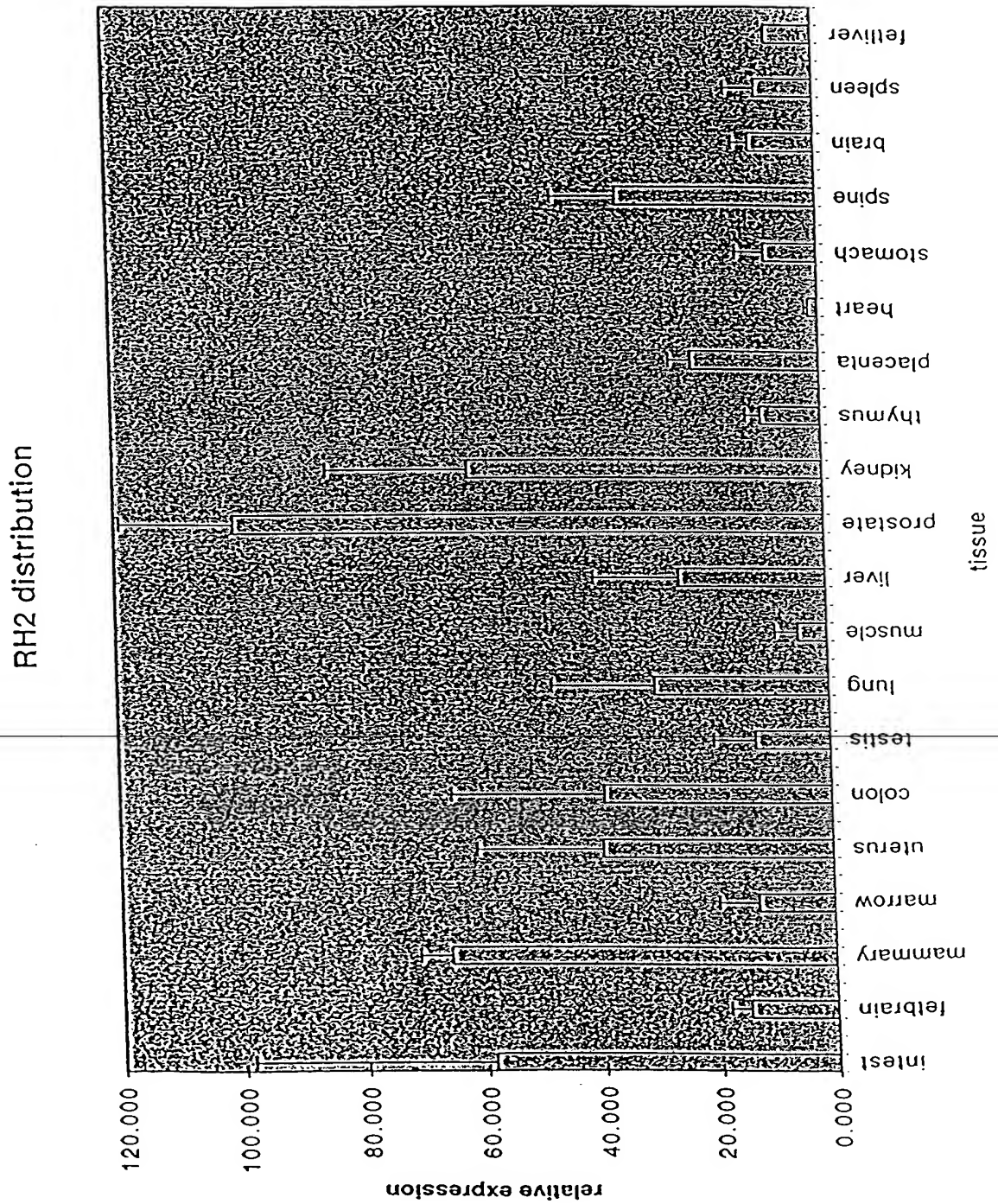
FIGURE 25

## IL17Rhom-1 Distribution



100000157 1030001

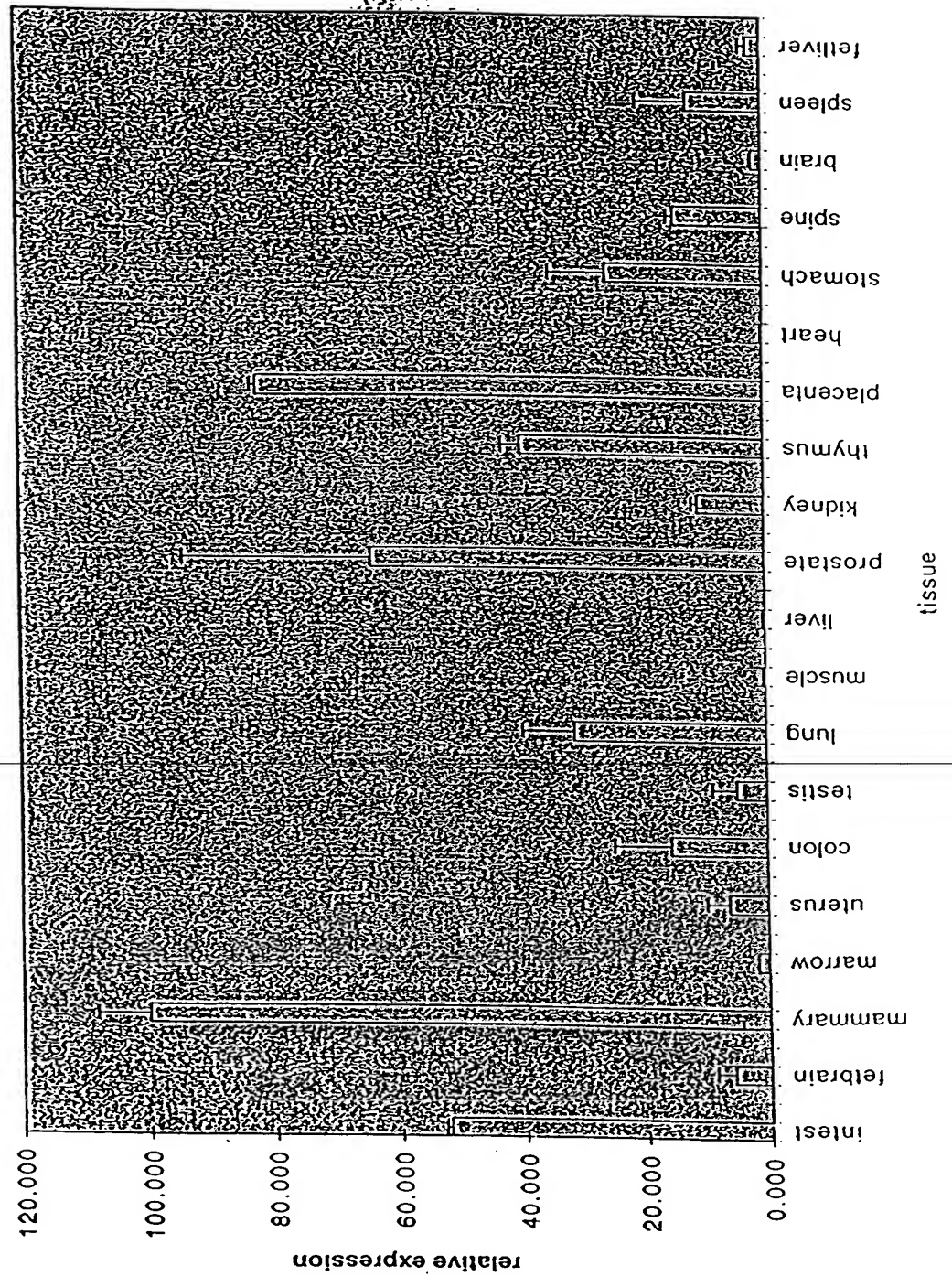
FIGURE 26



T00001" /5100001

FIGURE 27

RH3 distribution



T00E0T" 4ST0000T

## IL17 RH4 distribution

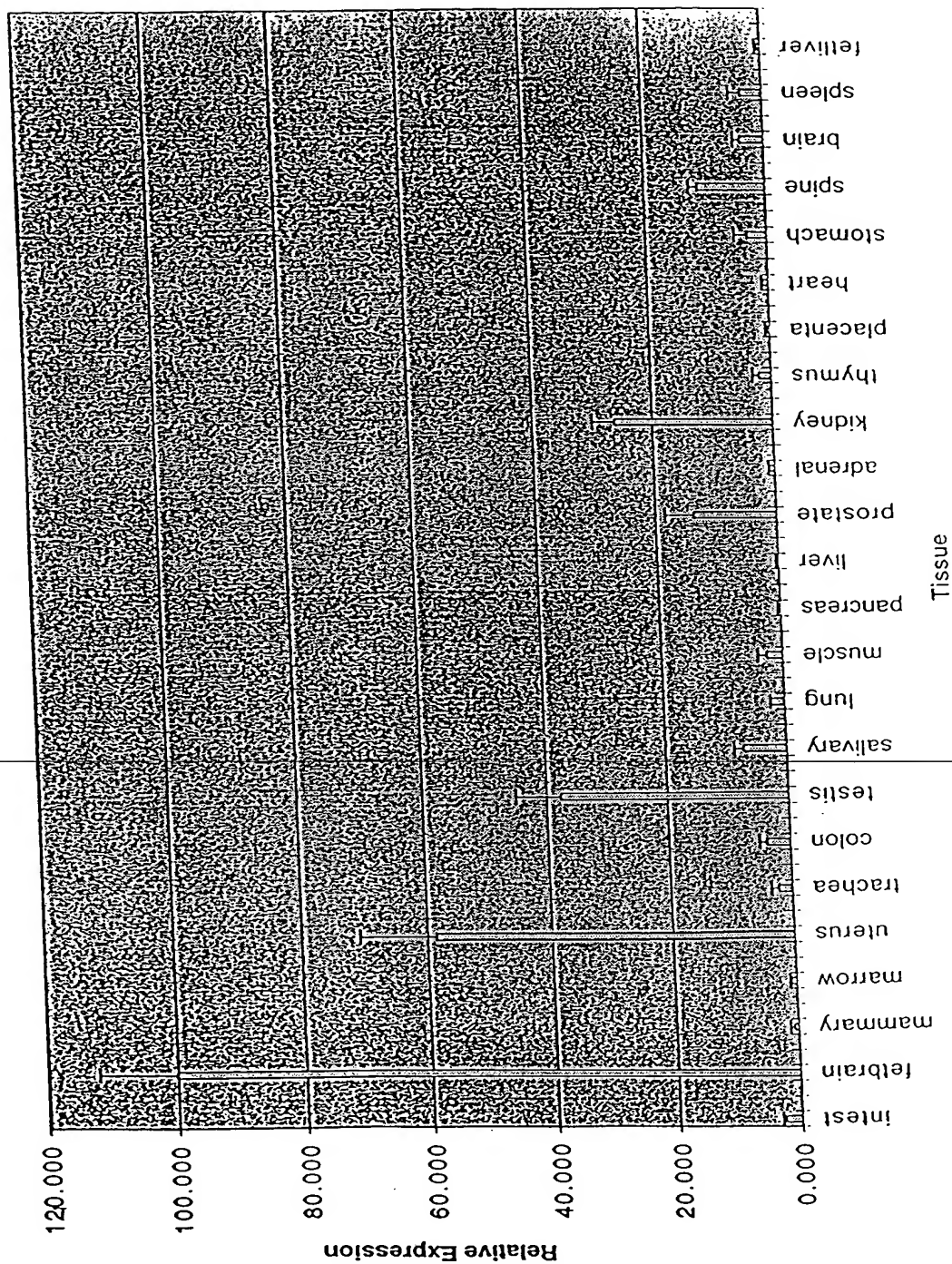
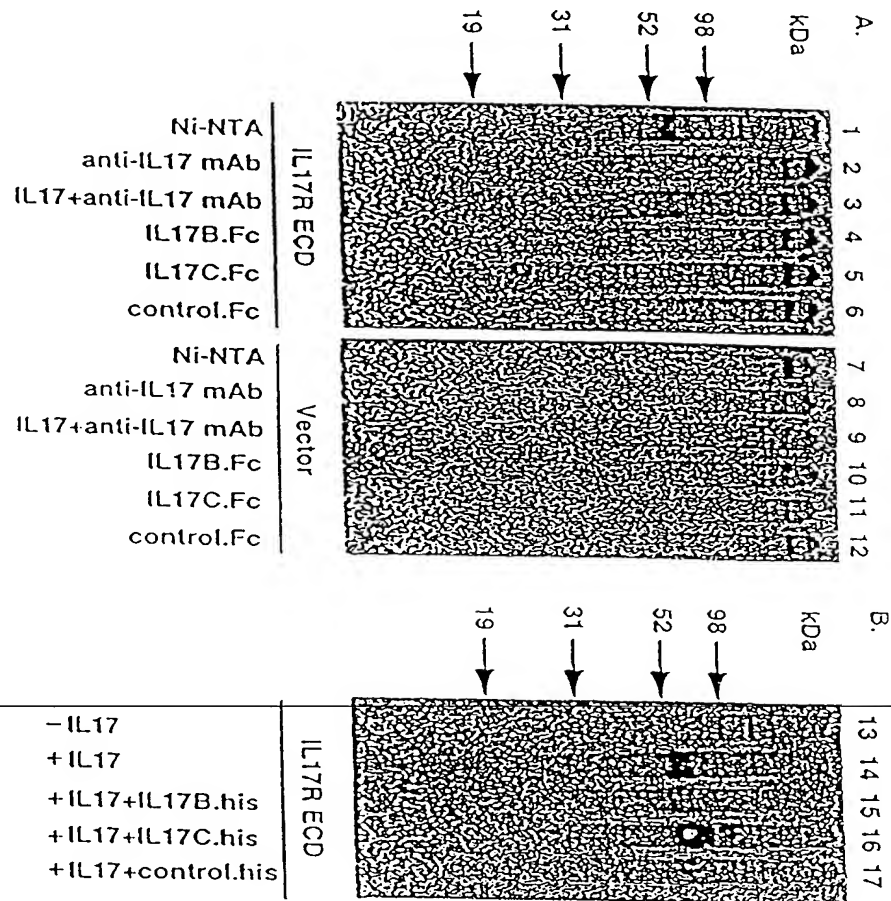




FIGURE 29



10000157, 103001

FIGURE 30

h-IL17 1 - - - - - M T P G K T S L V S L L L L S L E A I V K A G I T I P R - - - - -  
 h-IL17B 1 - - - - M D W P H N L L F L L T I S I F L G L G Q P R S P K S K R K G Q G R P G P - - - - -  
 h-IL17C 1 - - - - M T L L P G L L F L T W L H T C L A H H D P S L R G H P H S H G T P H C Y S A E E L P L G  
 h-IL17E 1 M R E R P R L G E D S S L I S L F L Q V V A F L A M V M G T H T Y S H W P S C C P - - - - -

h-IL17 30 - - - - - N P G C P N S E D K N F P R T V M V N L N I H N R N T N T N P K R - - - -  
 h-IL17B 39 A P G P H Q V P L D L V S R M K P Y A R M E E Y E R N I E E M V A Q L R N S S E L A O R K C E V N  
 h-IL17C 47 A P P H L L A R G A K W G O A L P V A L V S S L E A A S H R G R H E R P S A T T O C P V L R P E E  
 h-IL17E 42 - - - - - S K G Q D T S E E L L R W S T V P V P P L E P A R P N R H P E S C R A S E

h-IL17 63 - S S D Y Y N R S T S P W N L H R N E D P E R Y P S V I W E A K C R H L G C I N A D G - - N V D Y  
 h-IL17B 69 Q L W M S N K R S L S P W G Y S I N H D P S R I P V D L P E A R C L C L G C V N P F T M O E D R S  
 h-IL17C 97 L E A D T H Q R S I S P W R Y R V D T D E D R Y P Q K L A F A E C L C R G C I D A R T G - R E T A  
 h-IL17E 79 - D G P L N S R A I S P W R Y E L D R D L N R L P Q D L Y H A R C L C P H C V S L Q T G S H M D P

h-IL17 110 M N S V P I Q O E I L V L R R E - - - - - P P H C P N S F R L E K I L V S V G C T C V T P  
 h-IL17B 139 V S V P V F S Q V P V R R R L C P P P - - - - - P R T G P C R Q R A V M E T I A V G C T C I F -  
 h-IL17C 146 L N S V R L L Q S L L V L R R R P C S R D G S G L P T P G A F A F H T E F I H V P V G C T C V L P  
 h-IL17E 128 G N S E L L Y H N Q T V F Y R R P C H G E K - - - G T H K G Y C L E R R L Y R V S L A C V C V R P

h-IL17 151 V H H V A  
 h-IL17C 196 S V - - -  
 h-IL17E 175 V M G - -

10000157.103001

FIGURE 31A

100000157 10000000

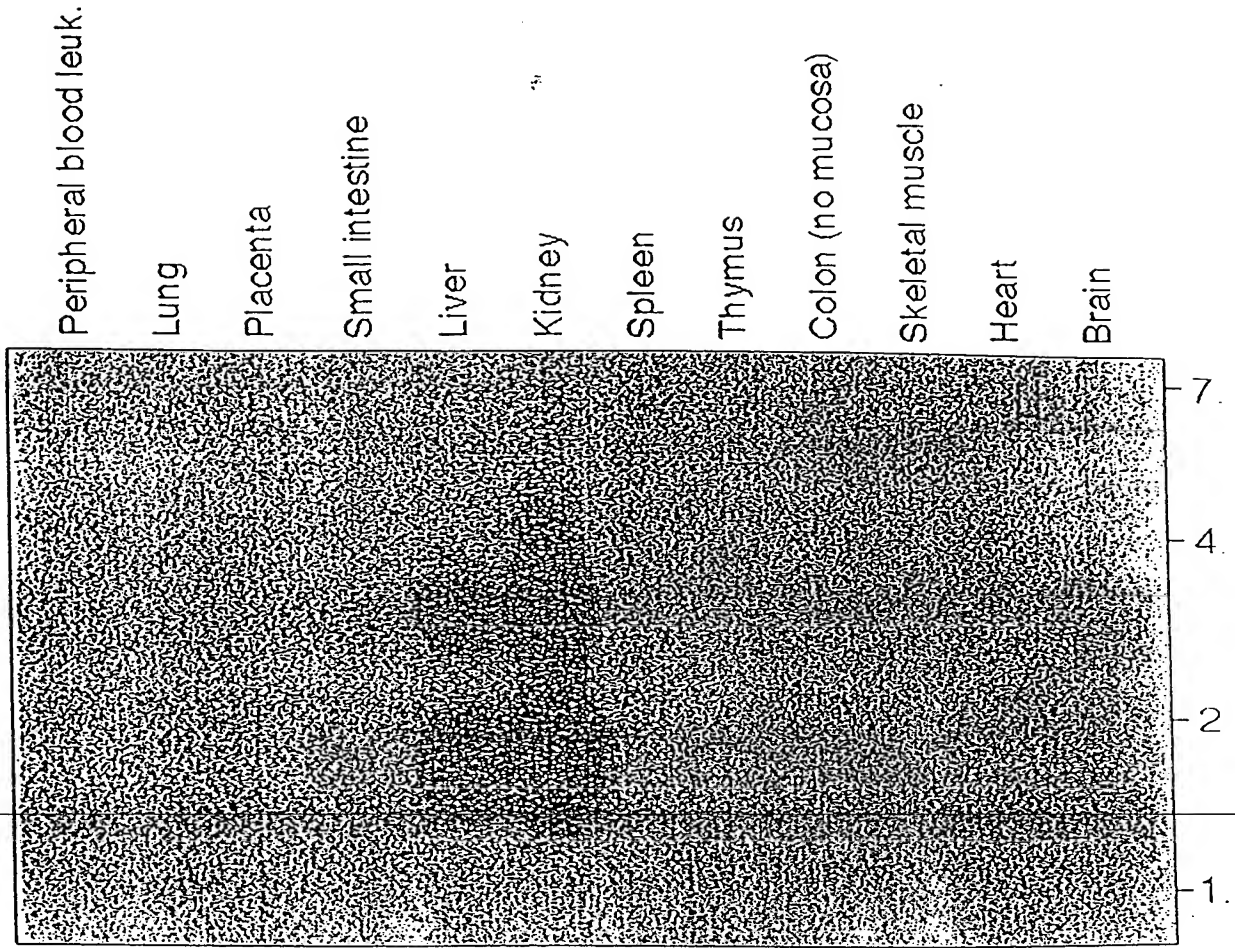


FIGURE 31B

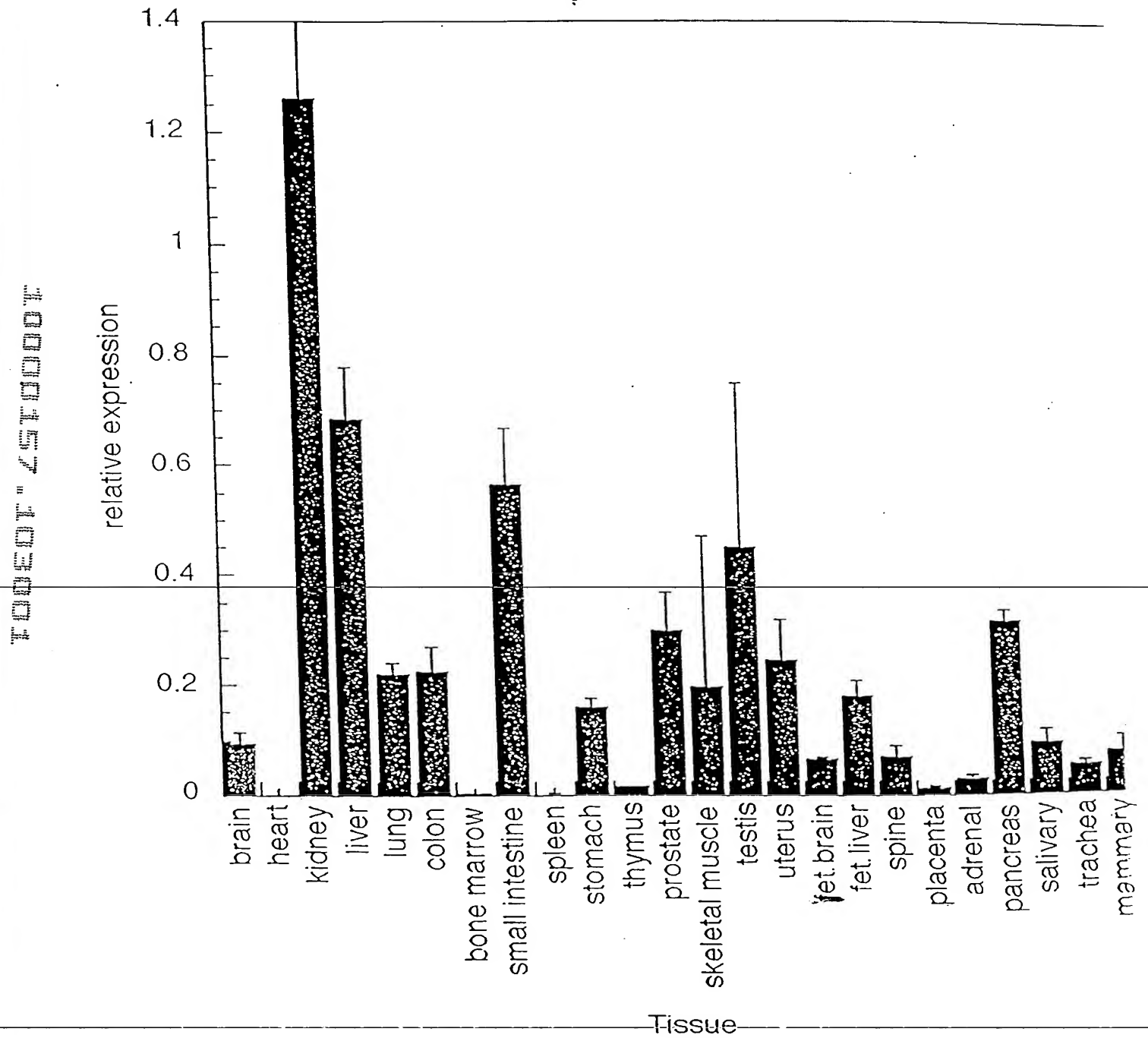




FIGURE 32A

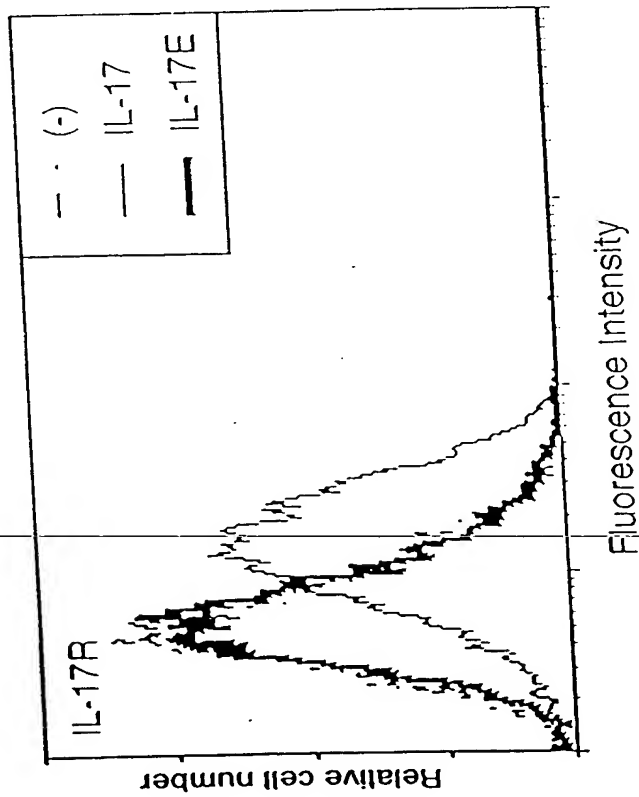
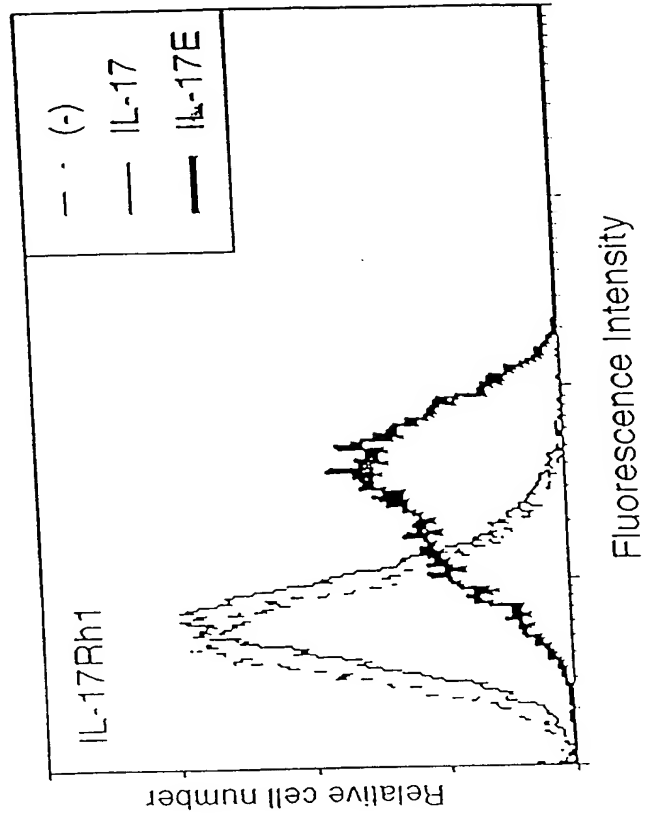
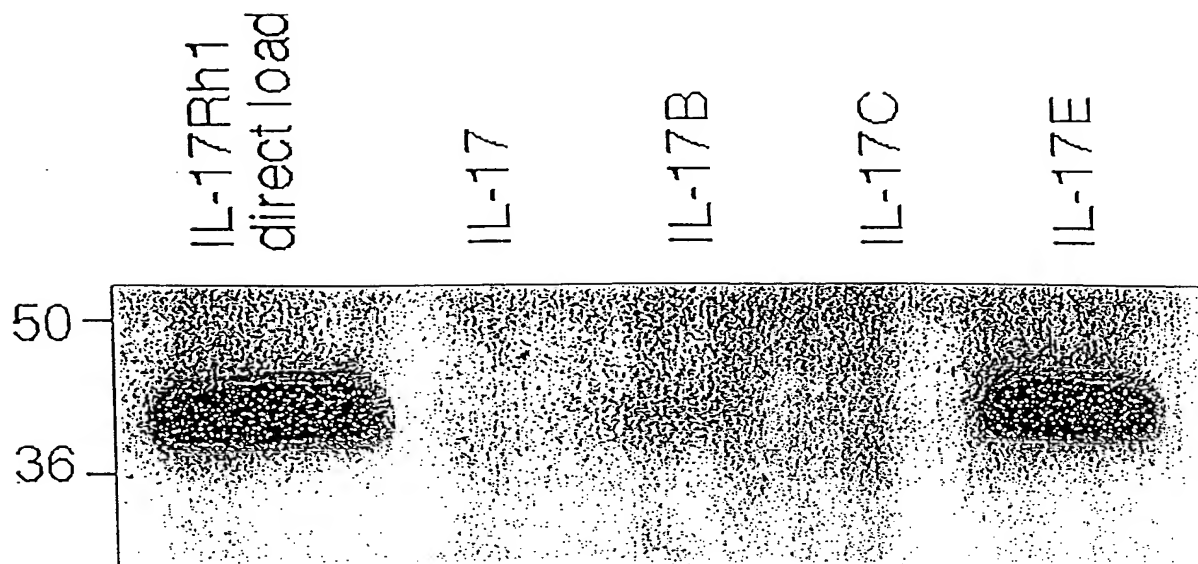


FIGURE 32B



FOOT" /STOOF

FIGURE 33

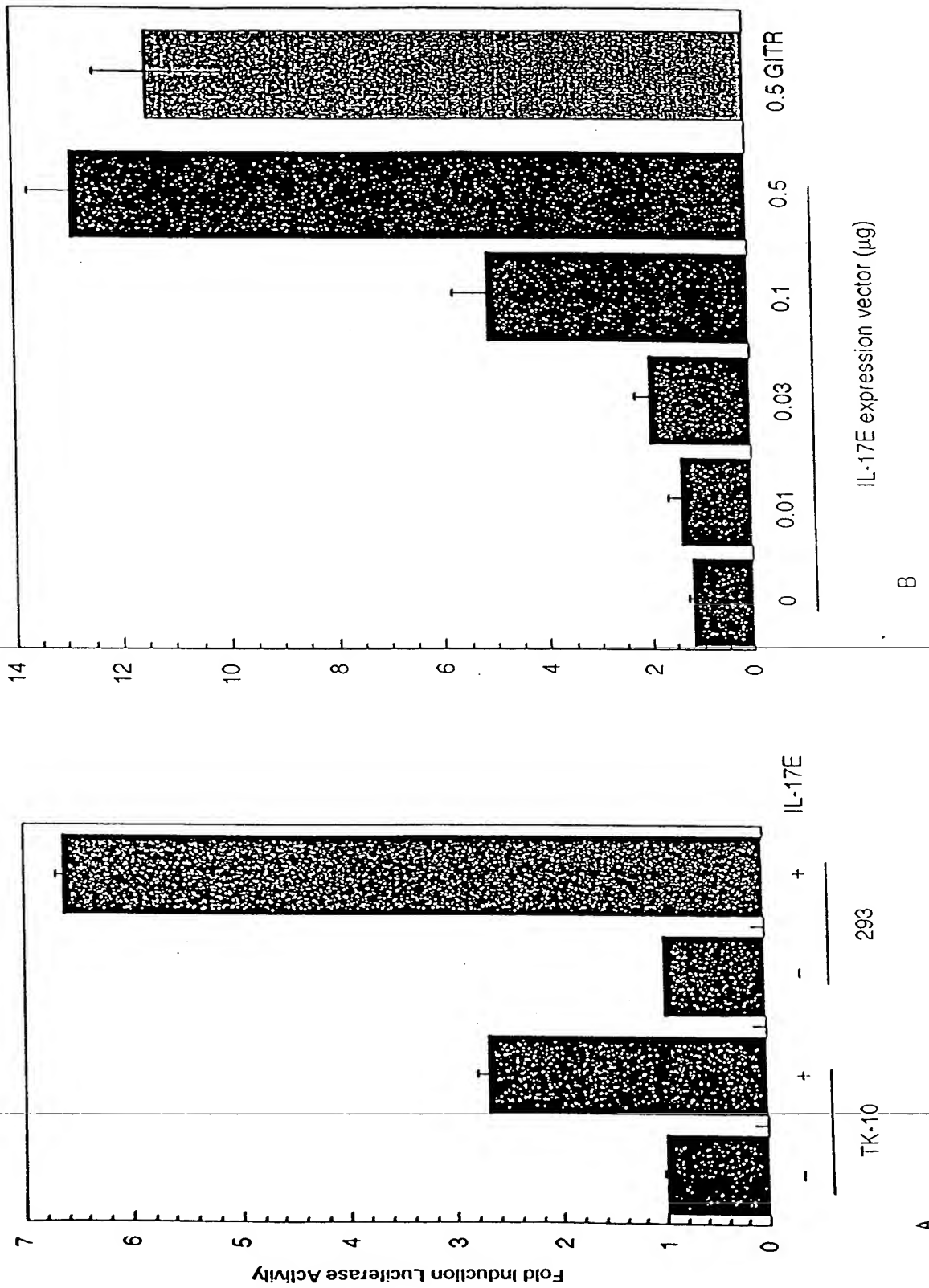


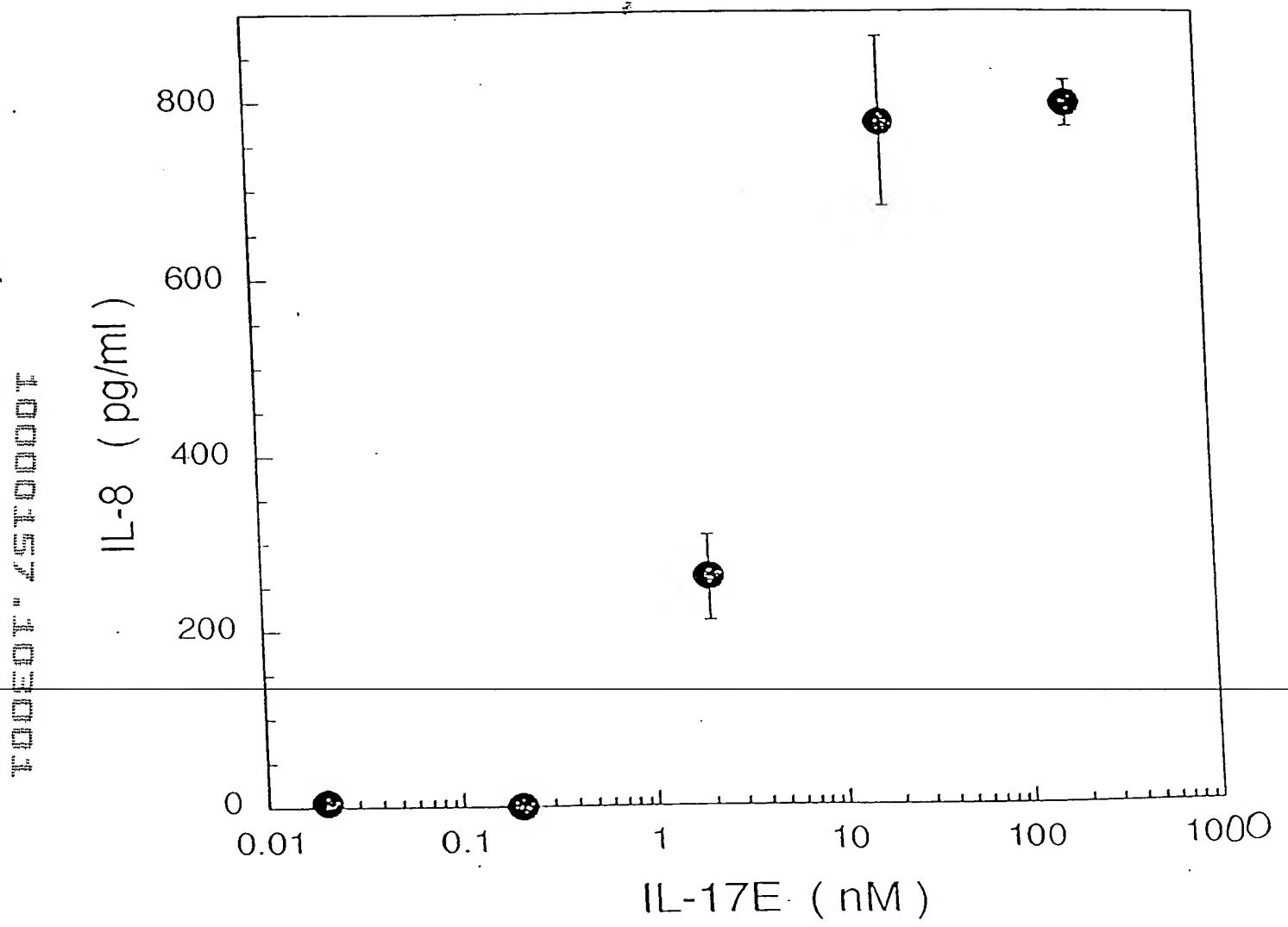
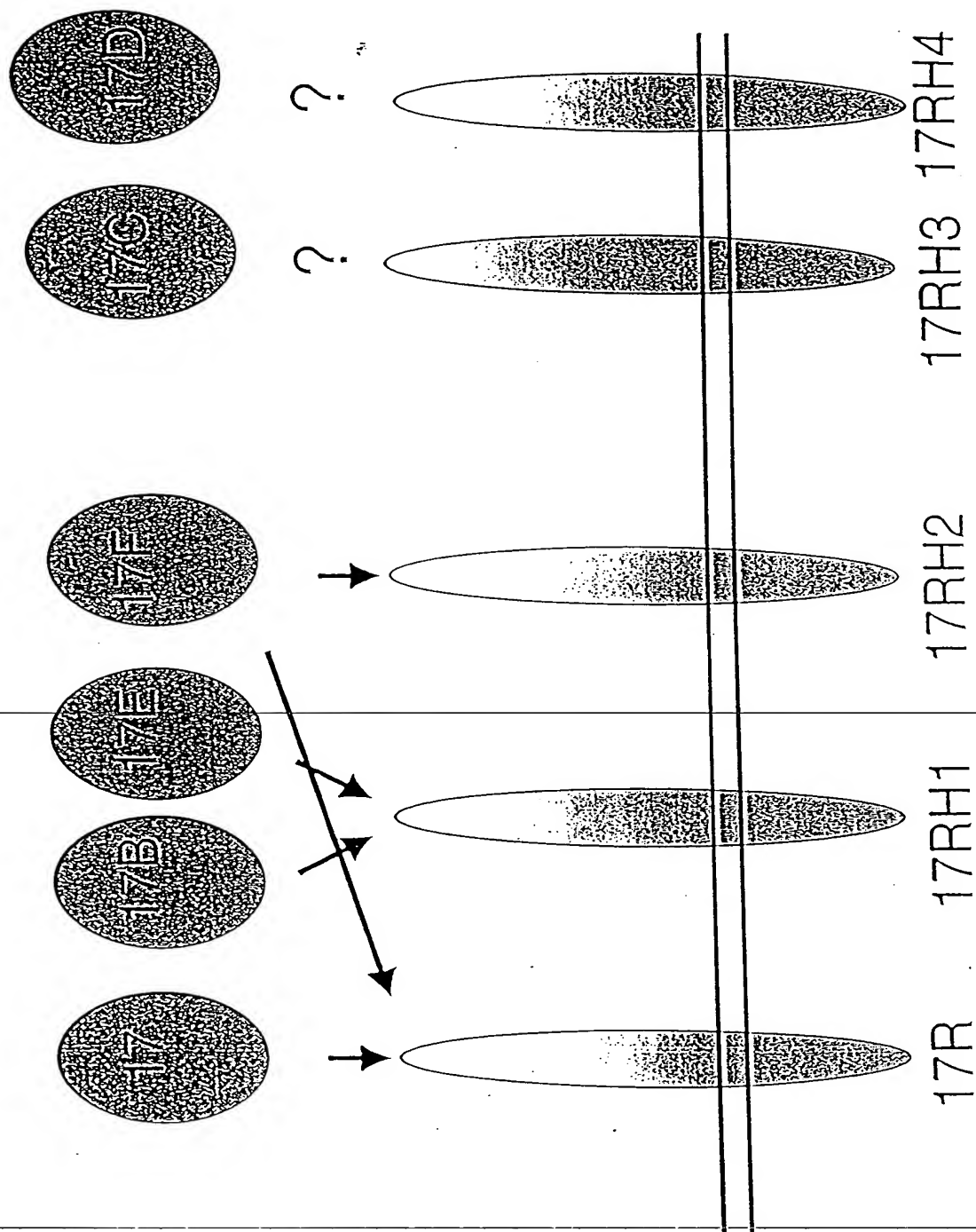
FIGURE 34

FIGURE 35

IL-17 family of cytokines has complex pattern  
of overlapping receptor-ligand specificities



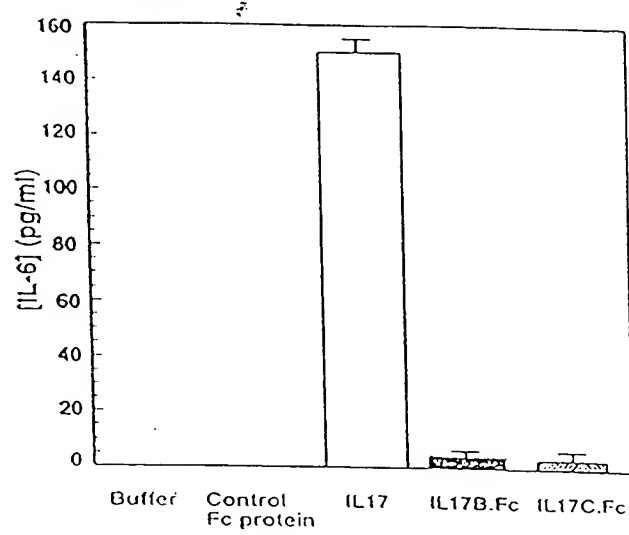
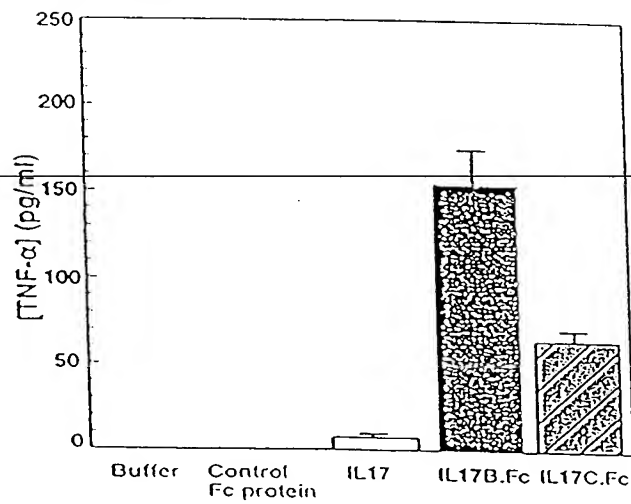
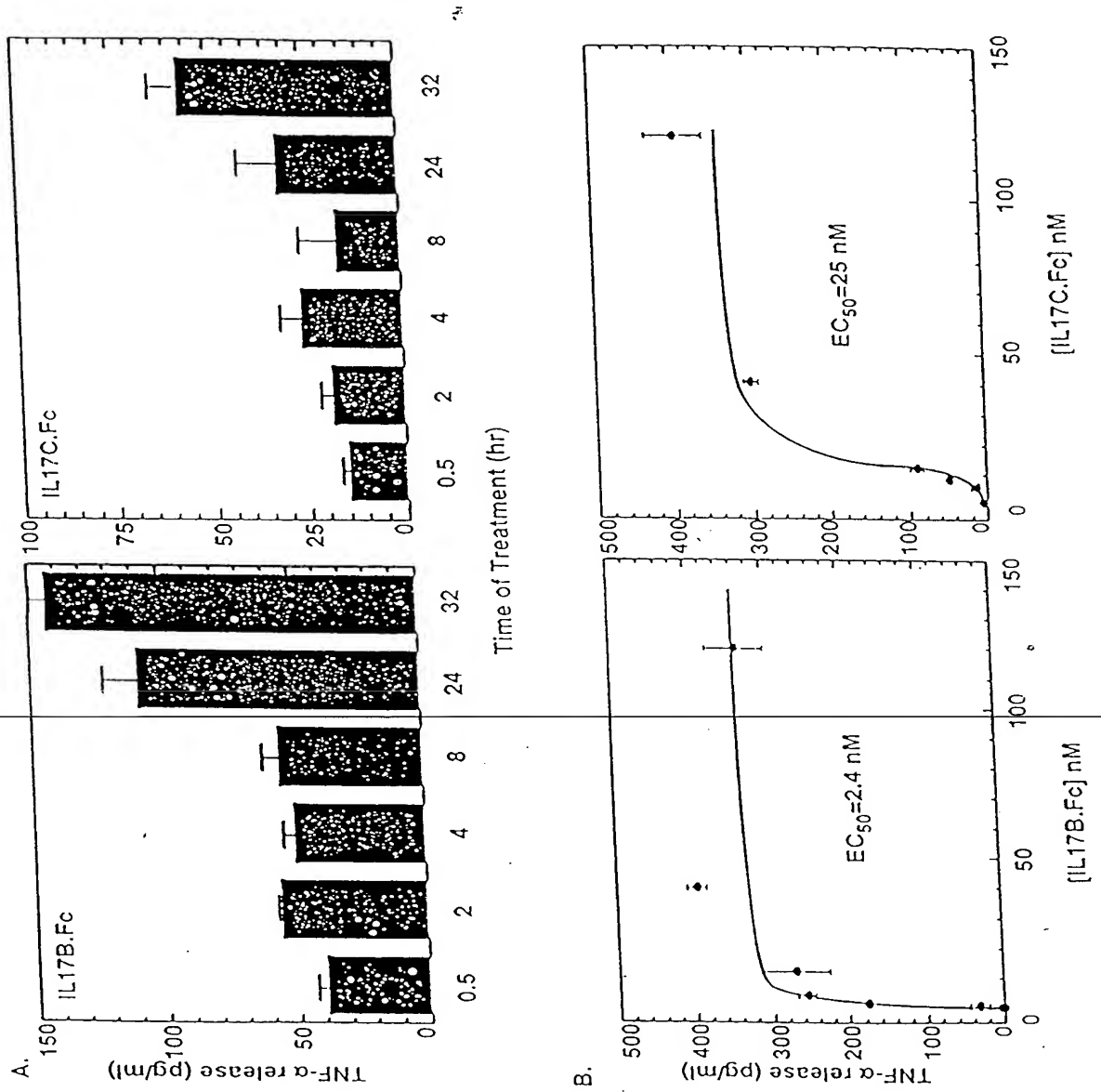
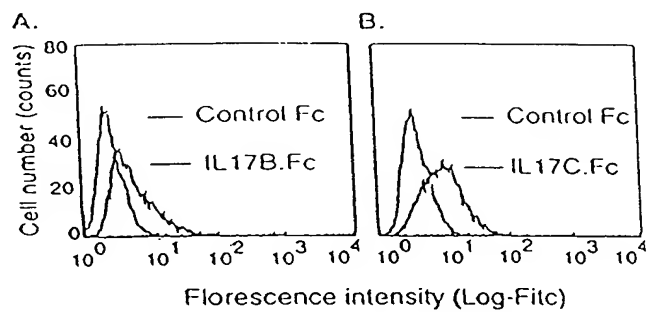
**FIGURE 36****A. HFF cells****B. THP1 cells**

FIGURE 37



**FIGURE 38**

10000157-103001



**FIGURE 39**

## IL-17 induces breakdown and inhibits synthesis of cartilage matrix

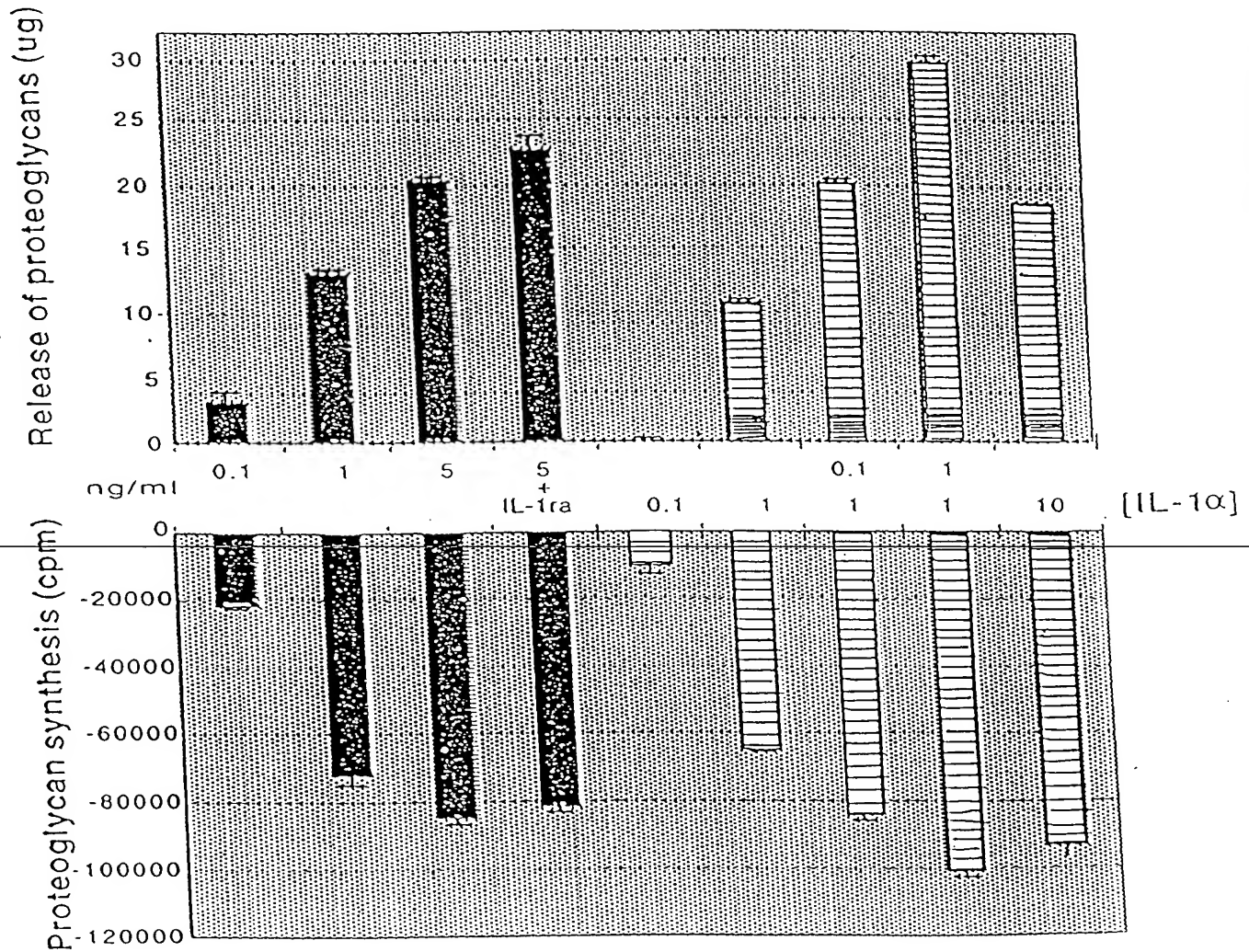
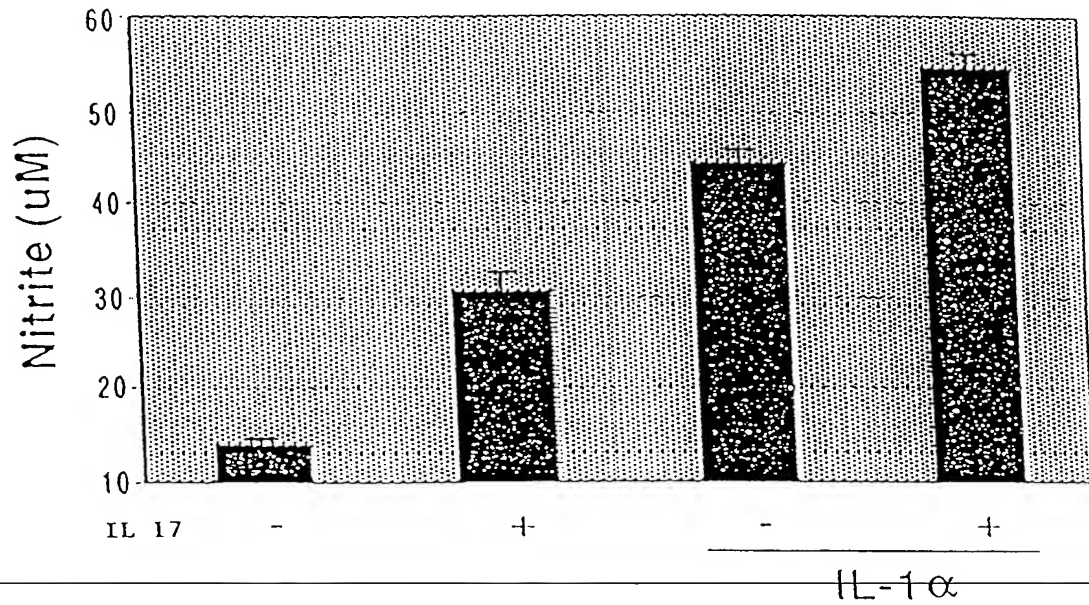


FIGURE 40

IL 17 increases basal and  
IL-1 $\alpha$ -induced nitric oxide release

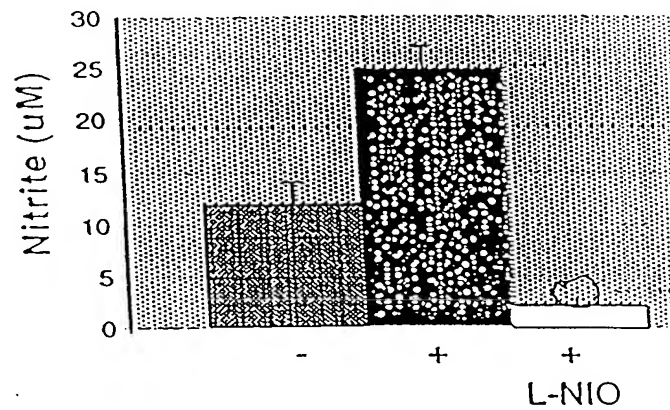


10000157 103001

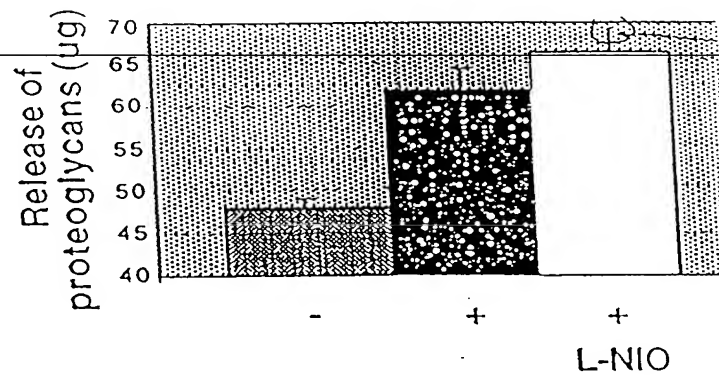
FIGURE 41

Inhibition of nitric oxide release does not block the detrimental effects of IL-17 on matrix breakdown or synthesis

A.



B.



C.

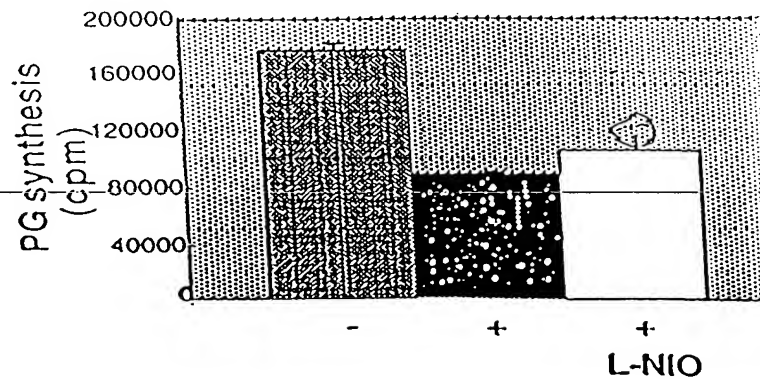
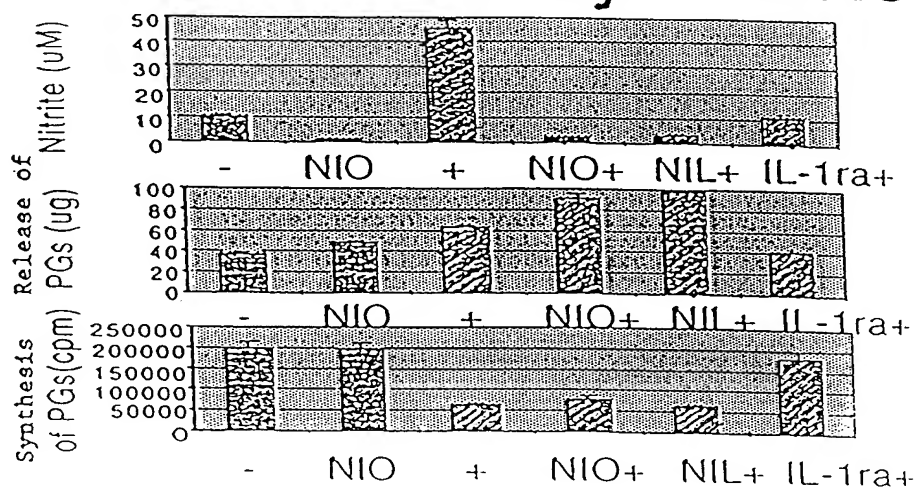


FIGURE 42

INHIBITION of NO release enhances  
 IL-1 $\alpha$ -induced matrix breakdown  
 but not matrix synthesis



10000157 103001

FIGURE 43

IL-17C

detrimental effects on articular cartilage

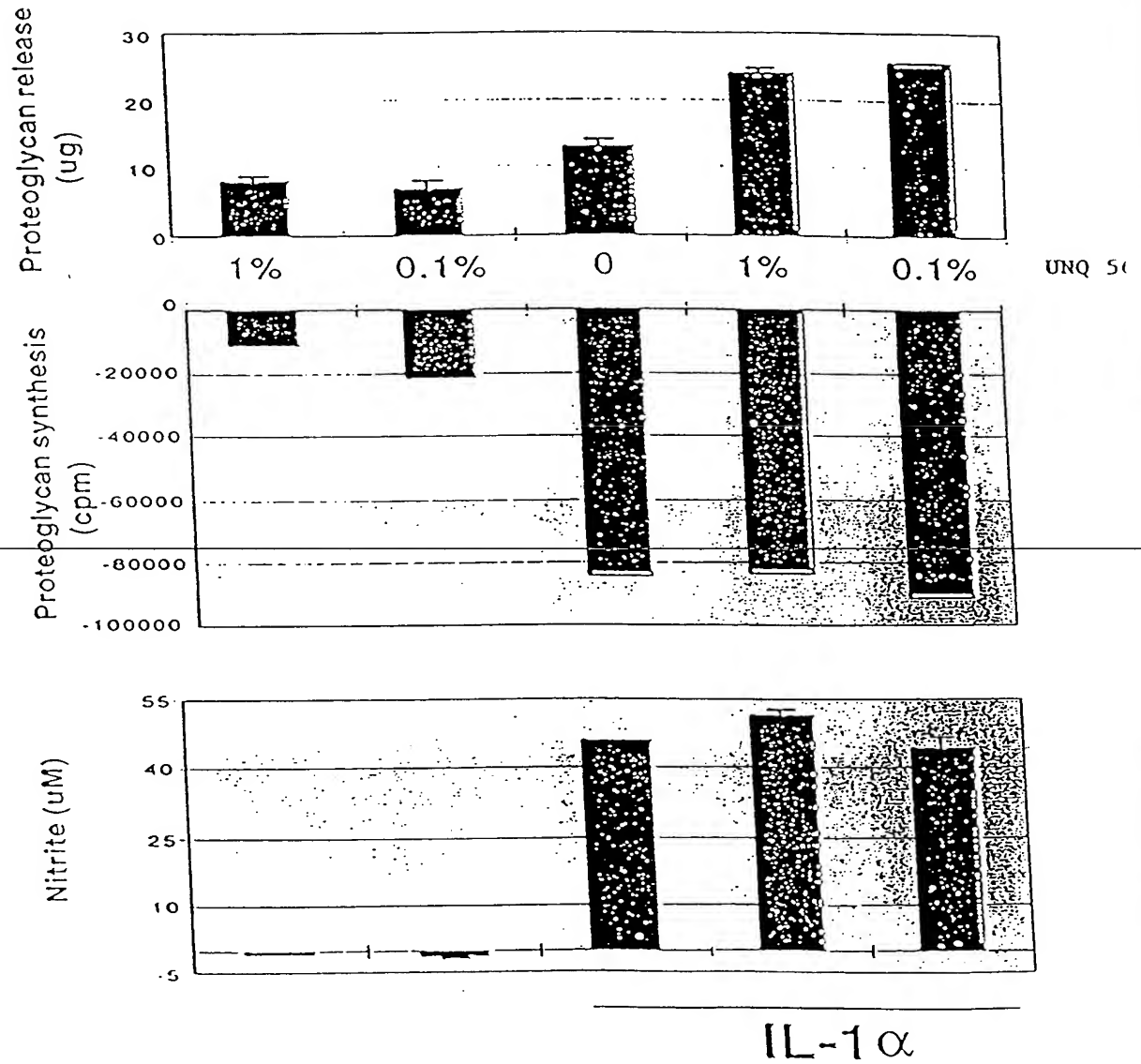
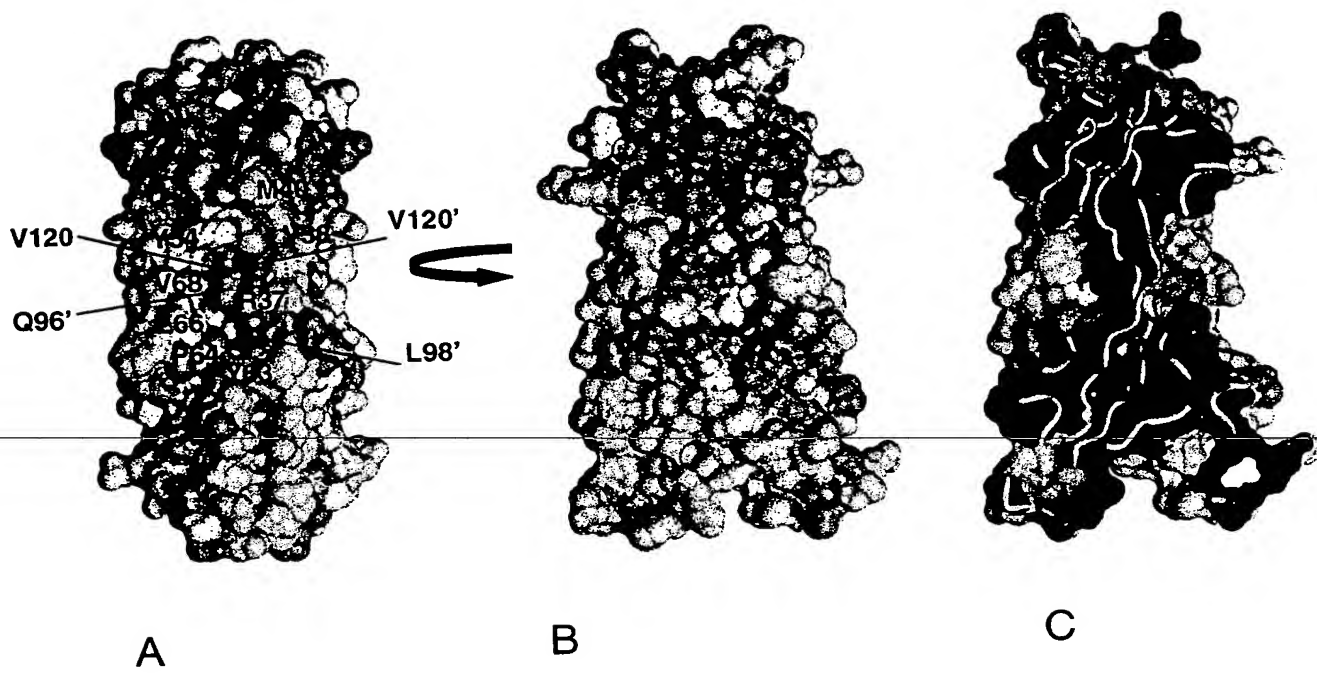


FIGURE 51



IL-17E is highly conserved between human and mouse

FIGURE 53

mIL-17E	1	-----	VAFLAM	IVGTHIVSLRIQEGC	SHL	PSCCPS	
nIL-17E	1	MRERPRLGEDSSLISLFLQVVAFLAM	VMGTHT	-----	YSHW	PSCCPS	
mIL-17E	35	KEQEPPEEMLKWSASVSPPE	ELSHTHAESCRASK	GGPLNSRAISPWSY			
nIL-17E	43	KGQDTSEELLRWSTVPVPPLE	PARPNRHPE	ESCRASE	GGPLNSRAISPWRY		
mIL-17E	85	ELDRDLNR	VPQDLYHARCLCPHC	VS	LQTGSHMDPL	GNSVPL	LYHNQTVFYR
nIL-17E	93	ELDRDLNR	LPQDLYHARCLCPHC	VS	LQTGSHMDPR	GNSSEL	LYHNQTVFYR
mIL-17E	135	RPCHGEE	STHRR	KCLERR	LYRVSLAC	VCVR	PRVMA
nIL-17E	143	RPCHGEK	STHKG	KCLERR	LYRVSLAC	VCVR	PRVMG





FIGURE 8

MLVAGFLLALPPSWAAGAPRAGRPARPRGCADRPEELLEQLYGRLAAGVLSAFHHTLQLGPREQARNASC  
PAGGRPGRDRFRPPTNLRSVSPWAYRISYDPARYPRYLPEAYCLCRGCLTGLFGCEEDVRFRSAPVYMPTVV  
LR RTPACAGGRSVYTEAYVTIPVGCTCVPEPEKDADSINSSIDKQGAKLLLGPNDA PAGP

Signal peptide:	Amino acids 1-15
N-glycosylation sites:	Amino acids 68-72;181-185
Tyrosine kinase phosphorylation site:	Amino acids 97-106
N-myristoylation sites:	Amino acids 17-23;49-55;74-80; 118-124
Amidation site:	Amino acids 21-25

10000157.103001

FIGURE 4

MTLLPGLLFLTWLHTCLAHHDPSLRGHPHSHGTPHCYSAEELPLGQAPPHLLARGAKWGQALPVALVSSLE  
AASHRGRHERPSATTQCPVLRPEEVLEADTHQRSISPWRYRVDTDEDYPQKLAFAECLCRGCIDARTGRE  
TAALNSVRLQLSLLVLRRLRRRPCSRDGSGGLPTPGAFAFHTEFIHVPVGCTCVLPRSV

Signal peptide:	Amino acids 1-18
Tyrosine kinase phosphorylation site:	Amino acids 112-121
N-myristoylation sites:	Amino acids 32-38;55-61;133-139
Leucine zipper pattern:	Amino acids 3-25
Homologous region to IL-17:	Amino acids 99-195

10000157 " 103001

FIGURE 6

MRERPRLGEDSSLISLFLQVVAFLAMVMGTHYSHWPSCCPKQDTSEELLRWSTVPVPPLEPARPNRHP  
ESCRASEDGPLNSRAISPWRYELDRDLNRLPQDLYHARCLCPHCVSLQTGSHMDPRGNSELLYHNQTVFYR  
RPCHGEKGTGTHKGYCLERRLYRVSLACVCVRPRVMG

Signal peptide:	Amino acids 1-32
N-glycosylation site:	Amino acids 136-140
Tyrosine kinase phosphorylation site:	Amino acids 127-135
N-myristoylation sites:	Amino acids 44-50;150-156

10000157-103001

**FIGURE 7**

**ATG**CTGGTAGCCGGCTTCCTGCTGGCGCTGCCGCCGAGCTGGGCGCGGGCGCCCCAGGGCGGGCAGGCG  
CCCCGCGCGGGCGCGGGGCTGCGCGGACCGGCCGGAGGAGCTACTGGAGCAGCTGTACGGGCGCCTGGCGG  
CCGGCGTGCTCAGTGCCTTCCACCACACGCTGCAGCTGGGGCCGCGTGAGCAGGCGCGCAACGCGAGCTGC  
CCGGCAGGGGGCAGGCCCCGGCGACCGCCGCTTCCGGCCGCCCCACCAACCTGCGCAGCGTGTCGCCCTGGGC  
CTACAGAATCTCCTACGACCCGGCGAGGTACCCAGGTACCTGCCTGAAGCCTACTGCCTGTGCCGGGGCT  
GCCTGACCGGGGCTGTTCCGGCGAGGAGGACGTGCGCTTCCGCAGCGCCCCTGTCTACATGCCCACCGTCGTC  
CTGCGCCGCACCCCCGCTGCGCCGGCGGCCGTTCCGTCTACACCGAGGCCTACGTCAACCATCCCCGTGGG  
CTGCACCTGCGTCCCCGAGCCGGAGAGAAGGACGCGACAGCATCAACTCCAGCATCGACAAACAGGGCGCCA  
AGCTCCTGCTGGGCCCCAACGACGCGCCCGCTGGCCCCCTGAGGCCGCTCCTGCCCCGGGAGGTCTCCCCGG  
CCCGCATCCCCGAGGCGCCCAAGCTGGAGCCGCTGGAGGGCTCGGTGCGCGACCTCTGAAGAGAGTGCACC  
GAGCAAACCAAGTGCCGGAGCACCAGCGCCGCTTTCCATGGAGACTCGTAAGCAGCTTCATCTGACACGG  
GCATCCCTGGCTTGCTTTTAGCTACAAGCAAGCAGCGTGCTGGAAGCTGATGGGAAACGACCCGGCACGG  
GCATCCTGTGTGCGGCCCGCATGGAGGGTTTGGAAAAGTTCACGGAGGCTCCCTGAGGAGCCTCTCAGATC  
GGCTGCTGCGGGTGCAAGGCGTGACTACCGCTGGGTGCTTGCCAAAGAGATAGGGACGCATATGCTTTTT  
AAAGCAATCTAAAAATAATAAAGTATAGCGACTATATACCTACTTTTAAATCAACTGTTTTGAATAGA  
GGCAGAGCTATTTTATATTATCAAATGAGAGCTACTCTGTTACATTTCTTAACATATAAACATCGTTTTTT  
ACTTCTTCTGGTAGAATTTTTTAAAGCATAATTGGAATCCTTGGATAAATTTTGTAGCTGGTACACTCTGG  
CCTGGGTCTCTGAATTCAGCCTGTCACCGATGGCTGACTGATGAAATGGACACGTCTCATCTGACCCACTC  
TTCCTTCCACTGAAGGTCTTCACGGGCCTCCAGGTGGACCAAAGGGATGCACAGGCGGCTCGCATGCCCCA  
GGGCCAGCTAAGAGTTCCAAAGATCTCAGATTTGGTTTTAGTCATGAATACATAAACAGTCTCAAACCTCGC  
ACAATTTTTTCCCCCTTTTGAAGCCACTGGGGCCAATTTGTGGTTAAGAGGTGGTGAGATAAGAAGTGGA  
ACGTGACATCTTTGCCAGTTGTCAGAAGAATCCAAGCAGGTATTGGCTTAGTTGTAAGGGCTTTAGGATCA  
GGCTGAATATGAGGACAAAGTGGGCCACGTTAGCATCTGCAGAGATCAATCTGGAGGCTTCTGTTTTCTGCA  
TTCTGCCACGAGAGCTAGGTCCTTGATCTTTTCTTTAGATTGAAAGTCTGTCTCTGAACACAATTATTTGT  
AAAAGTTAGTAGTTCTTTTTTAAATCATTAAGAGGCTTGCTGAAGGAT

10000157.103001

# Inflammatory Bowel Disease: Expression of IL-17 Family in Mouse Model of IBD

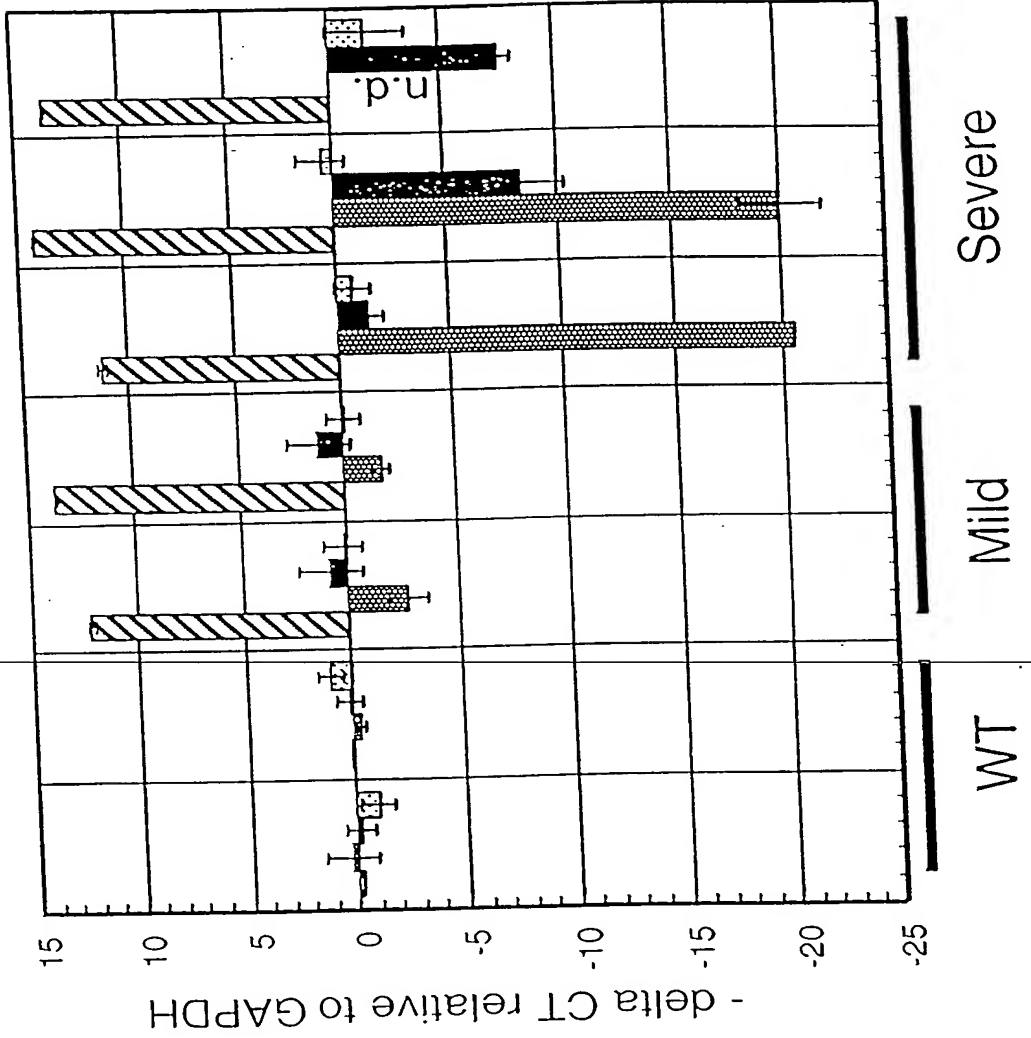
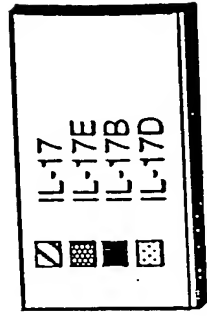


FIGURE 44

IL-17D, present in brain, decreases rapidly following stroke

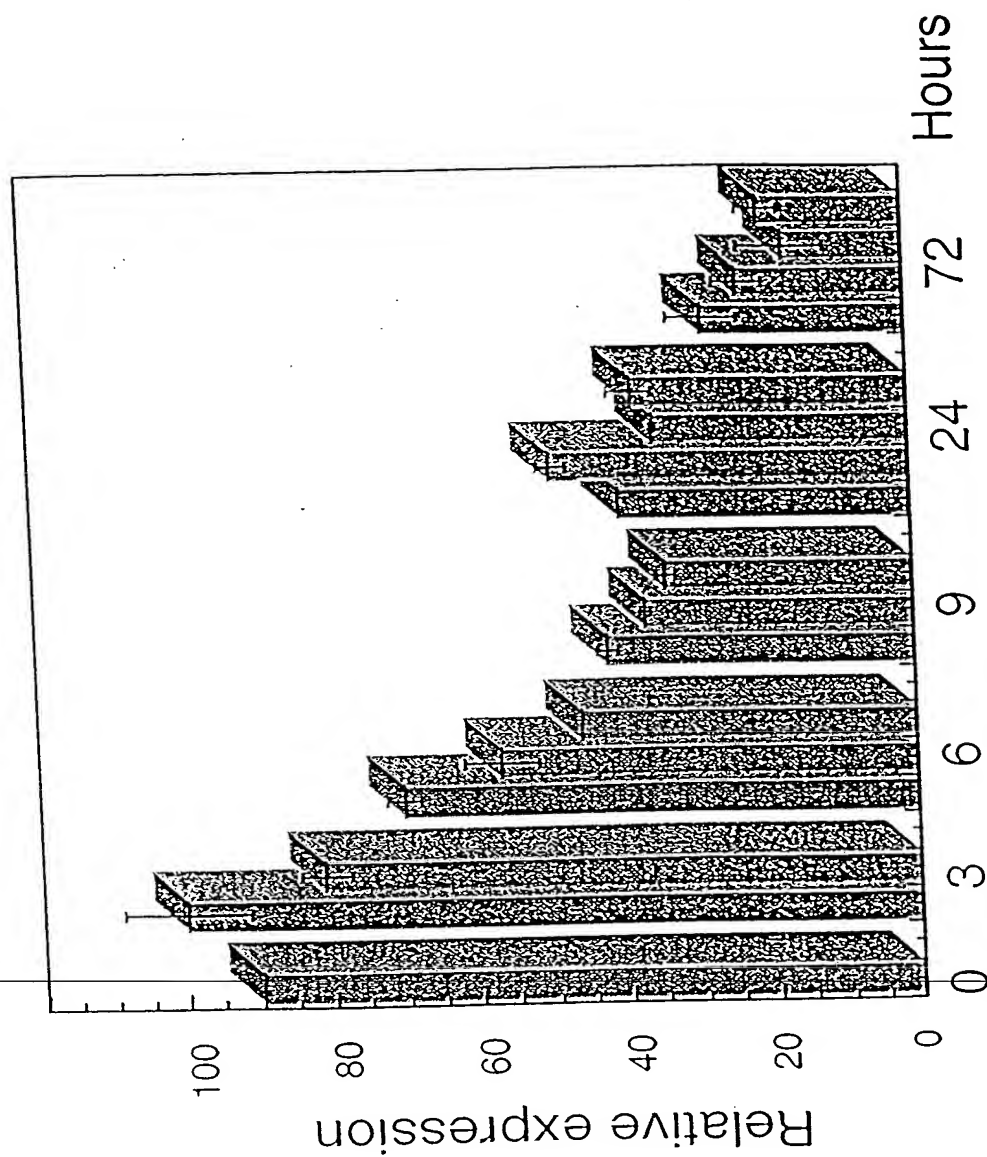
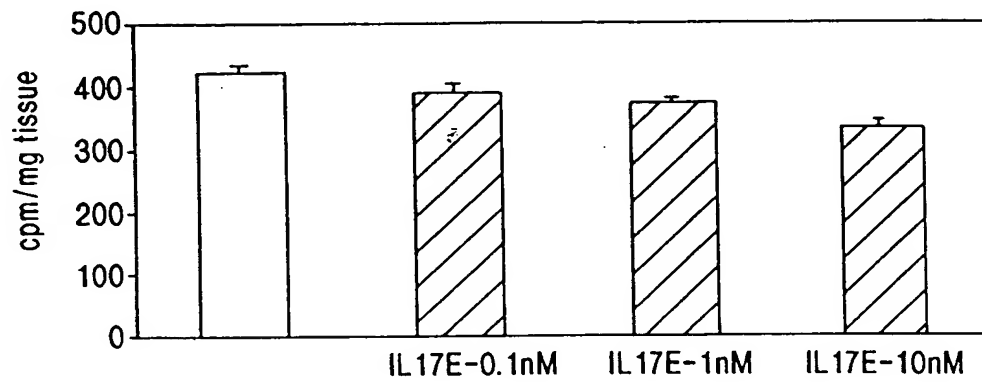
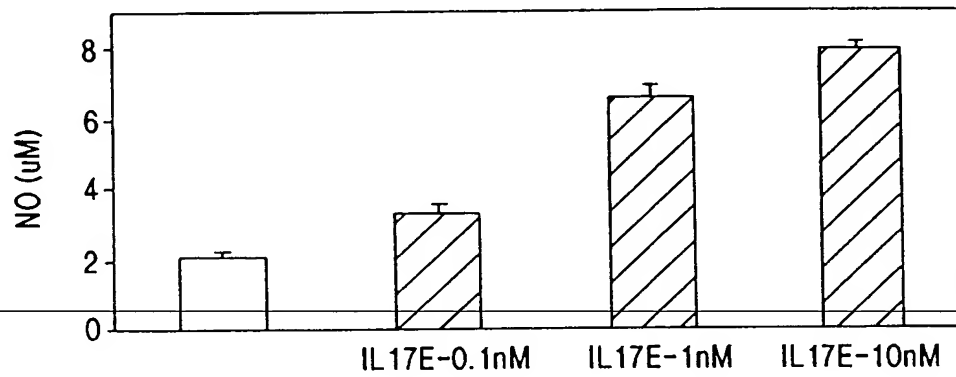
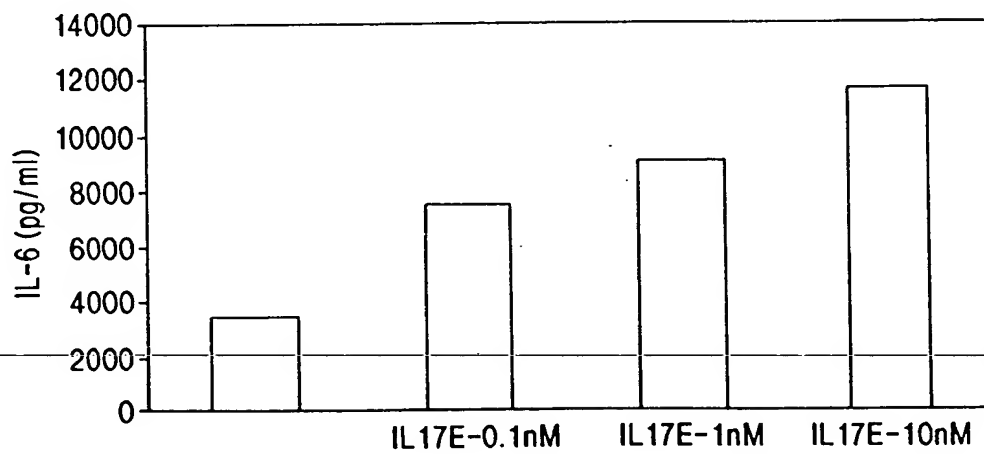
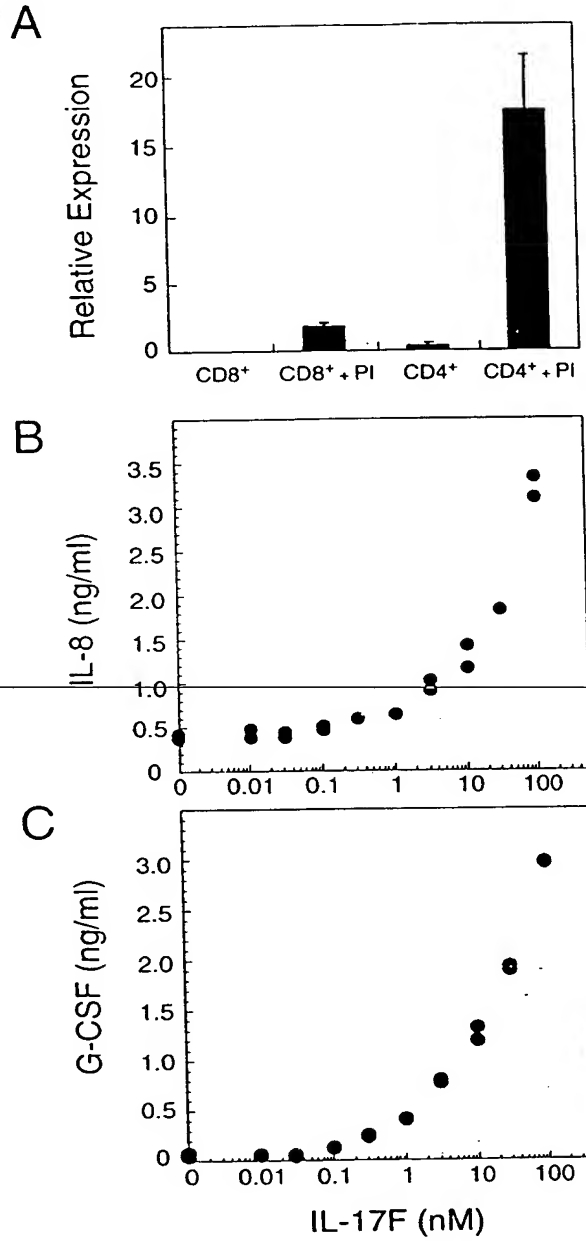
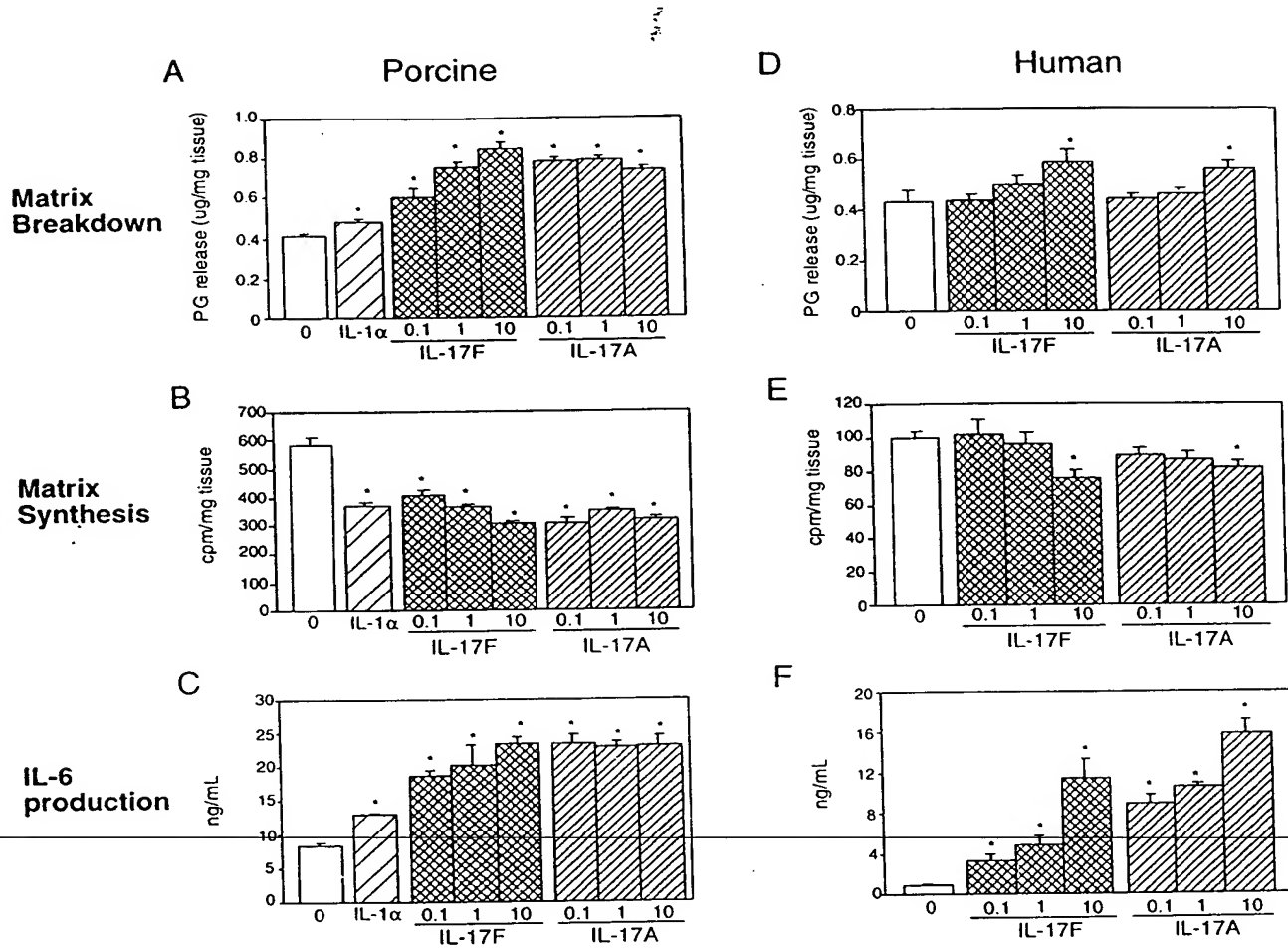


FIGURE 45

**FIGURE 46****FIG. 46A****FIG. 46B****FIG. 46C**

**FIGURE 47**



**FIGURE 48**

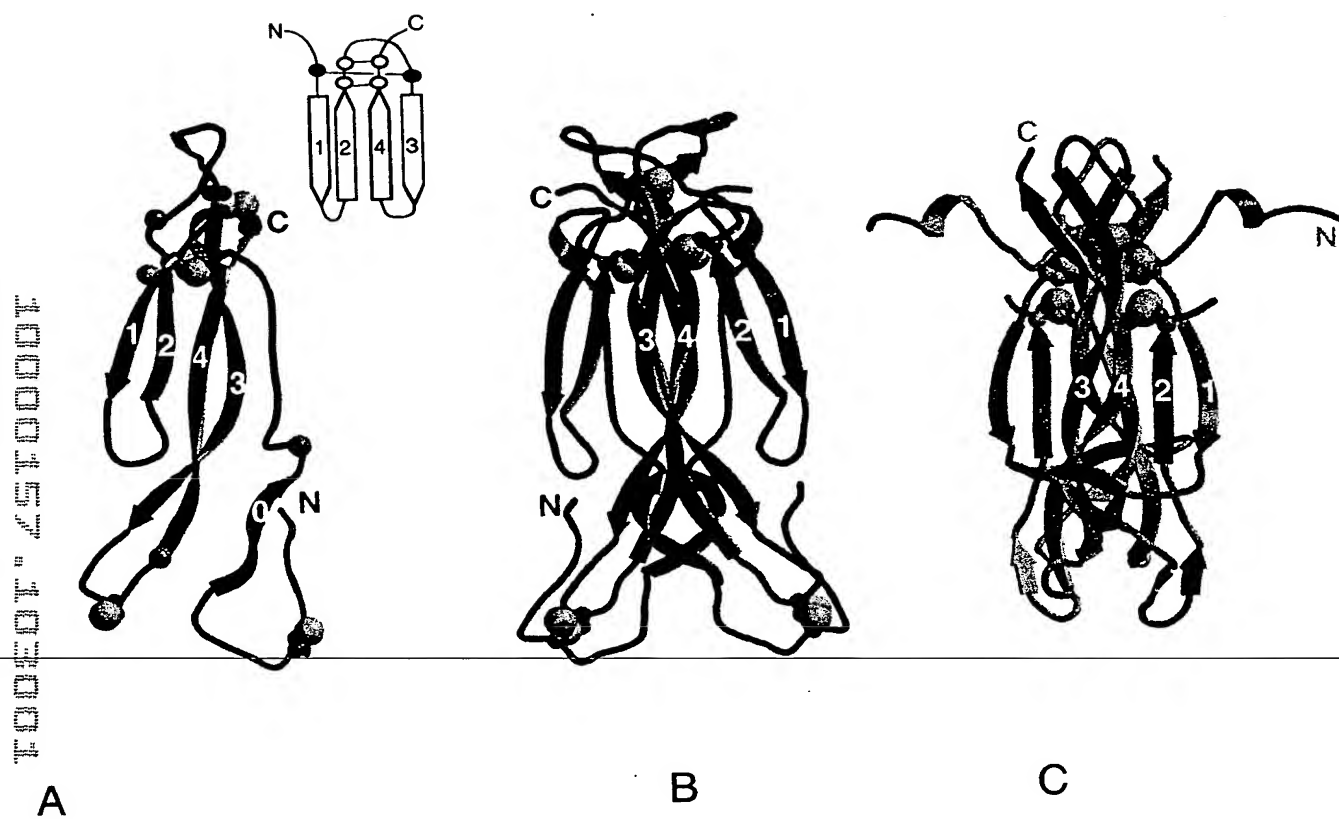
**FIGURE 49**

FIGURE 50

IL-17F	.....	.....	.....	.....RKIPKVG	HTFFQKPES	17
IL-17A	.....	.....	.....	.....IVKAG	ITIPRNP.G	14
IL-17B	.....QPRS	PKSKRKGQGR	PGPLAPGPHQ	VPLDLVSRMK	PYARMEEYER	44
IL-17C	HHDPSLRGHP	HSHGTPHYS	AEELPLGQAP	PHLLARGAKW	GQALPVALVS	50
IL-17E	.....	.....	.....YS	HWPS-PSKG	QDTSEELLRW	22

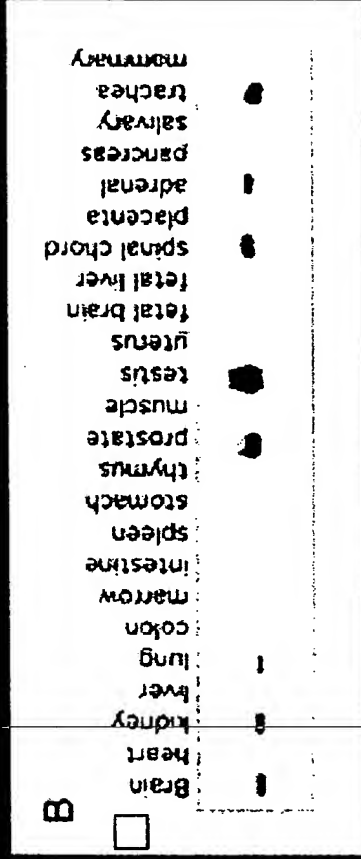
		0			1	
IL-17F	PPVPGG....	....SMKLDI	GIINENQRV	MSRNIESRST	PWNYTVTWD	59
IL-17A	PNSDKNFPR	TVMVNLNIHN	RNTNTN..PK	RSSDYNNRST	PWNLHRNED	62
IL-17B	NIEEMVAQLR	..NSSELAQR	K-EV....NL	QLWMSNKRSL	PWGYSINH	88
IL-17C	SLEAASHRGR	..HERPSATT	Q-PVLRPEEV	LEADTHQRSI	PWRYRVDTD	98
IL-17E	STVPVPPLP	..ARPNRHPE	S-RASE....	.DGPLNSRAI	PWRYELDRD	65

		2		3	
IL-17F	PNRYPSEVVQ	AQ RNLG IN	A..QGKEDIS	MN VPI.QQE	TLVVRRKHQG 106
IL-17A	PERYPSVIWE	AK RHLG IN	A..DGNVDYH	MN VPI.QQE	ILVLRREPPH 109
IL-17B	PSRIPVDLPE	AR L LG VN	PF.TMQEDRS	MV VPV.FSQ	VPVRRR...L 133
IL-17C	EDRYPQKLAF	AE L RG ID	AR.TGRETA	LN VRL.LQS	LLVLR...RP 144
IL-17E	LNRLPQDLYH	AR L PH VS	LQTGSHMDPR	GN ELLYHNQ	TVFYRRP... 112

			4	
IL-17F	SV.....	....SFQLEK	VL..VTVG T	VTPVIHHVQ ... 133
IL-17A	PN.....	....SFRLEK	IL..VSVG T	VTPIVHHVA ... 136
IL-17B	PPPPRTGP.	....RQRA	VMETIAVG T	IF..... ... 160
IL-17C	SRDGSGGLPT	PGAFAFHTEF	IH..VPVG T	V.LPRSVAA ALE 184
IL-17E	HGEKGTHKG	.....Y LER	RLYRVSLA V	VRPRVMG... ... 145

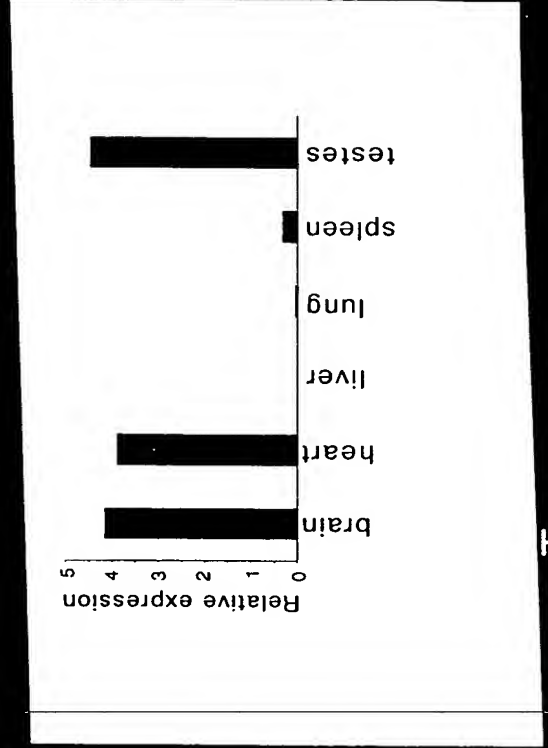
10000157 100001

# Tissue distribution of IL-17E



Human

## IL-17E (PCR then probed with cDNA)



Mouse

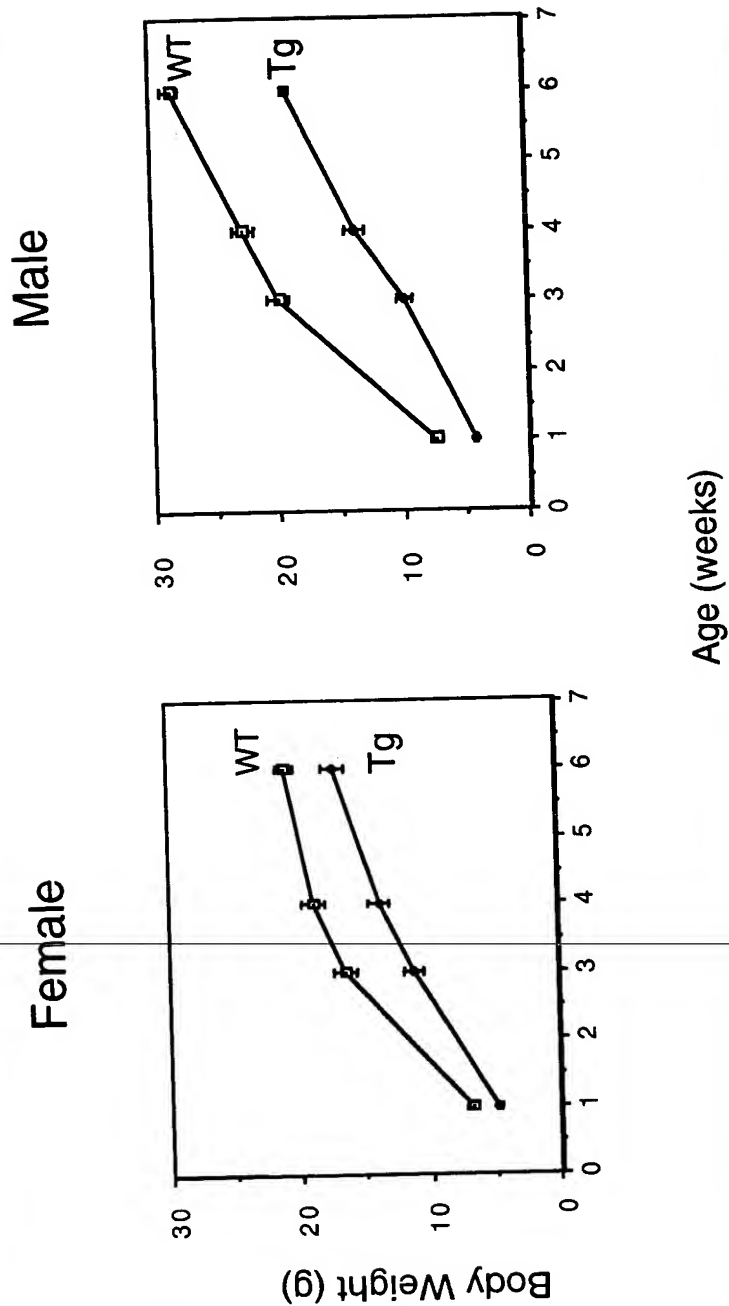
Taqman assay

FIGURE 54

# mIL-17E transgenics are growth retarded

FIGURE 55

57/70



IL17E transgenics are jaundiced by 6 weeks of age

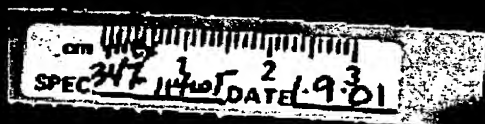
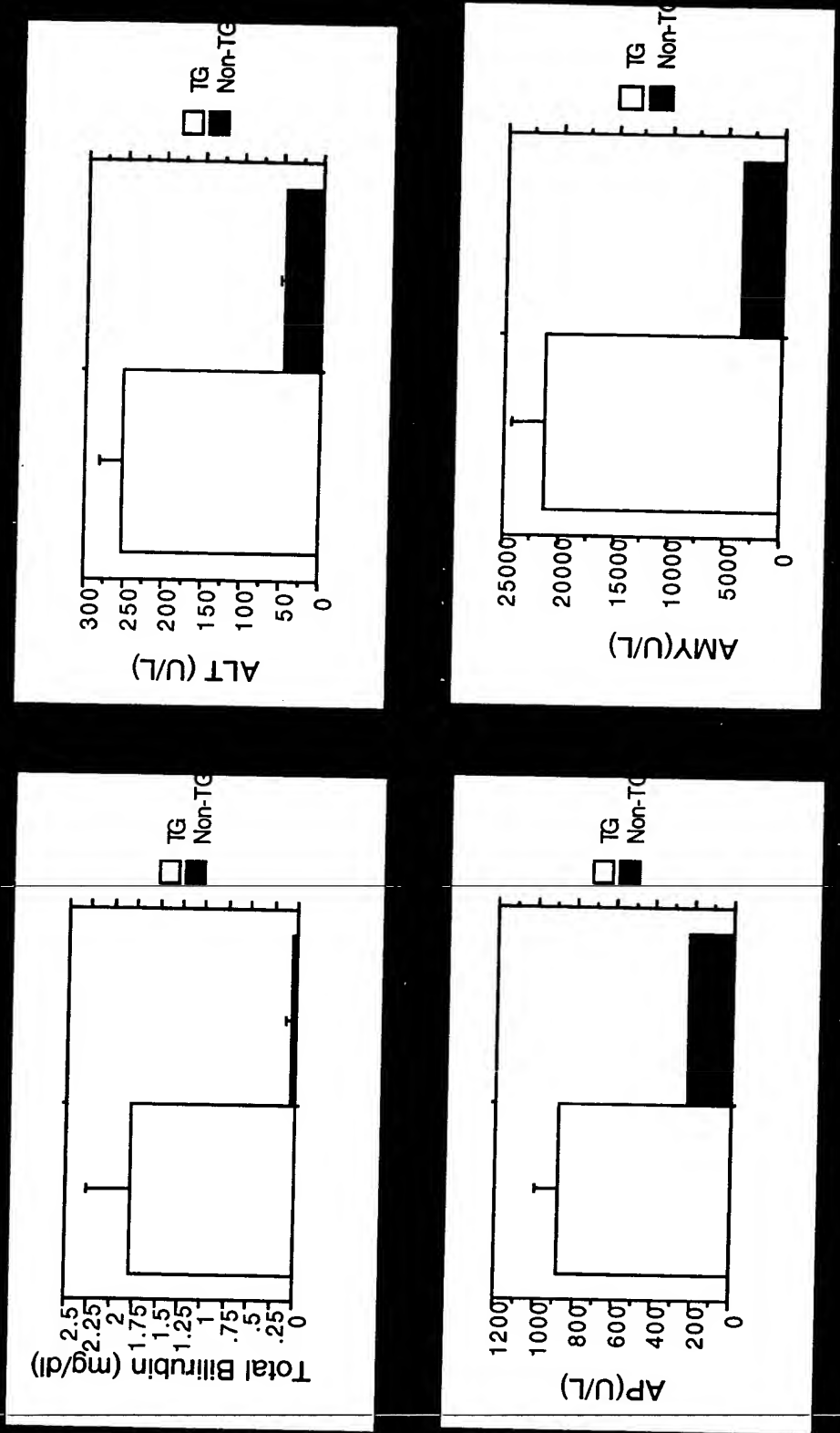


FIGURE 56

FIGURE 57

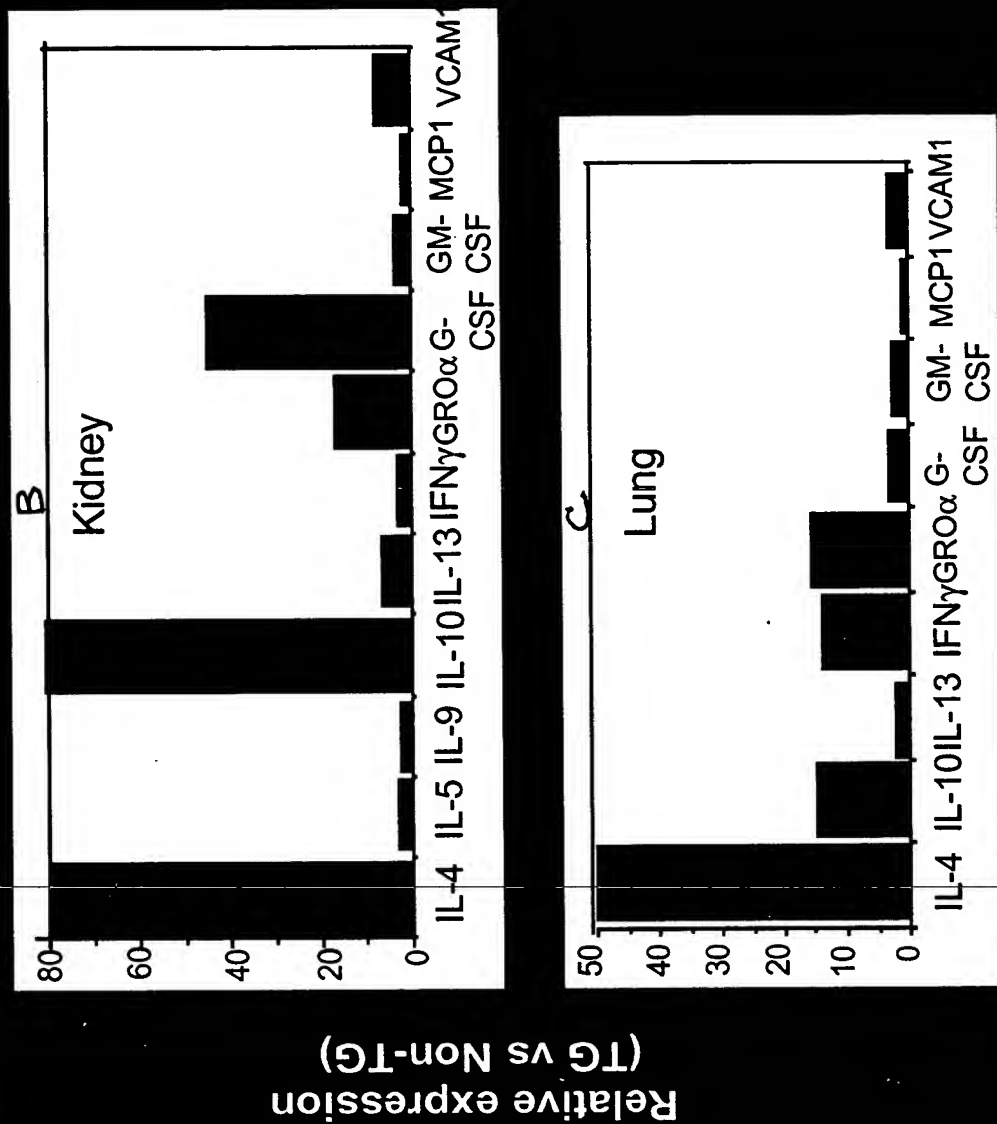
mL-17E transgenics have elevated  
total bilirubin and liver enzymes







FIGURES 58B - 58C



# Gene profiling of L-17E transgenics (Taqman)

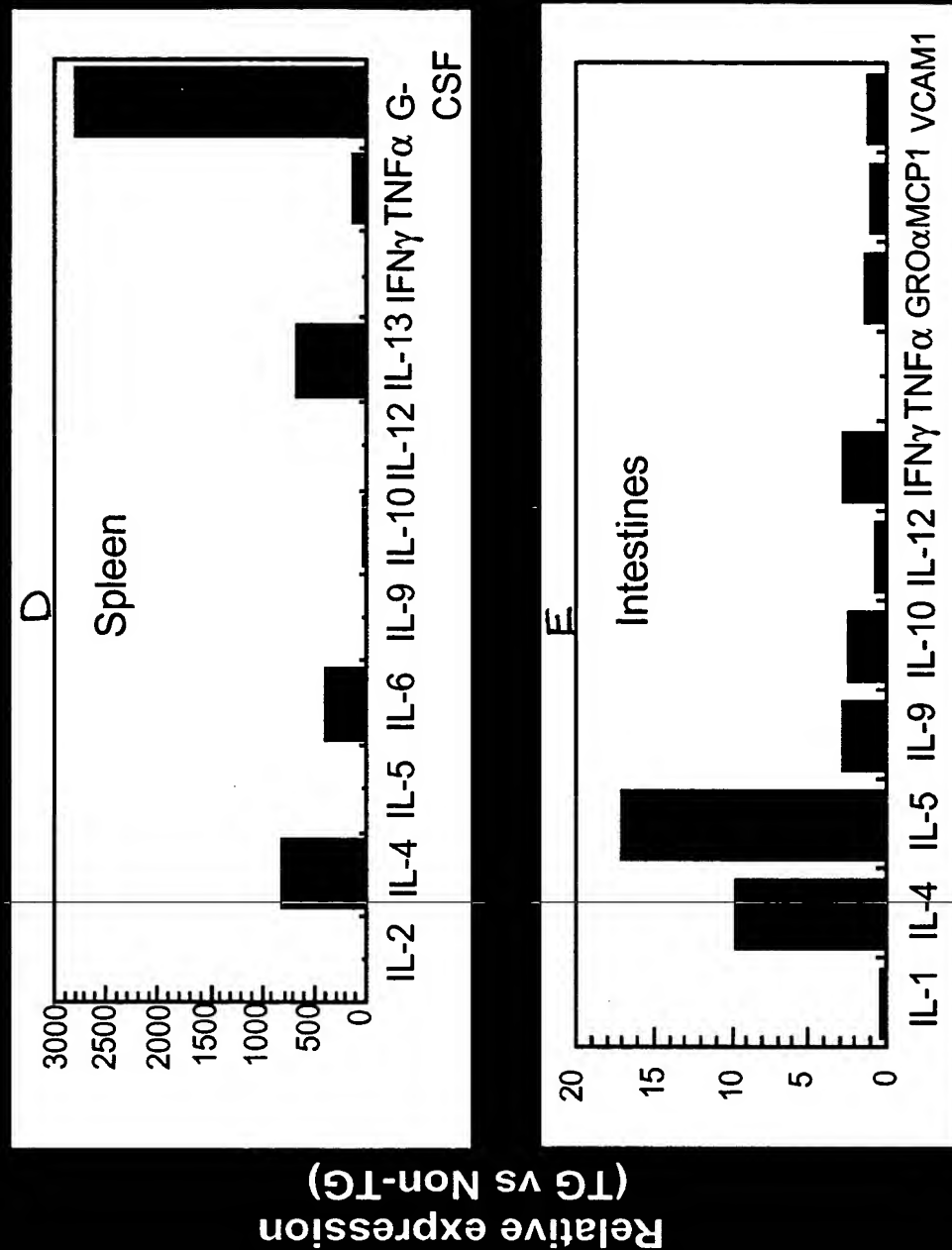


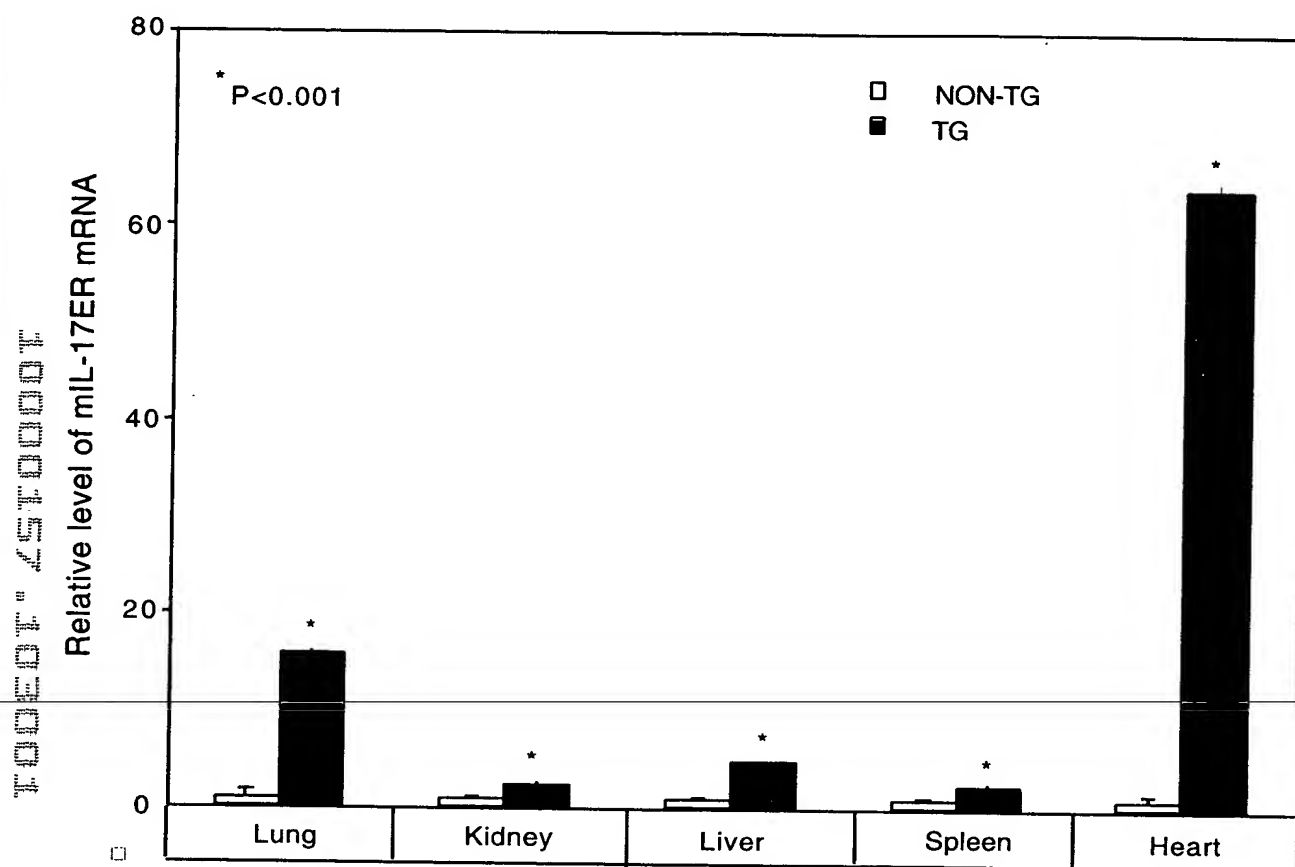
FIGURE 59

FIGURE 60

Elevated serum IL-5, IL-13 and TNF  $\alpha$   
in mIL-17E transgenics

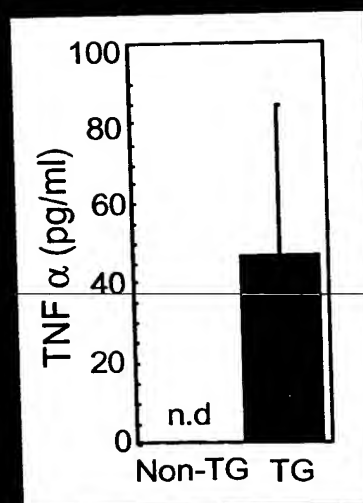
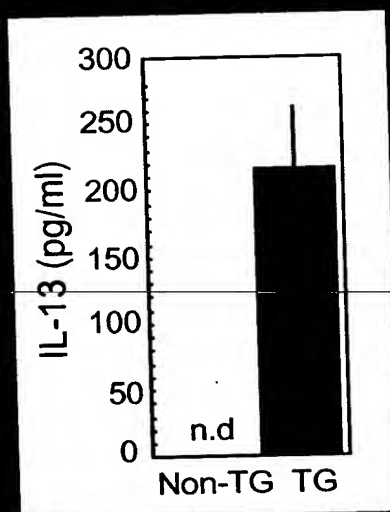
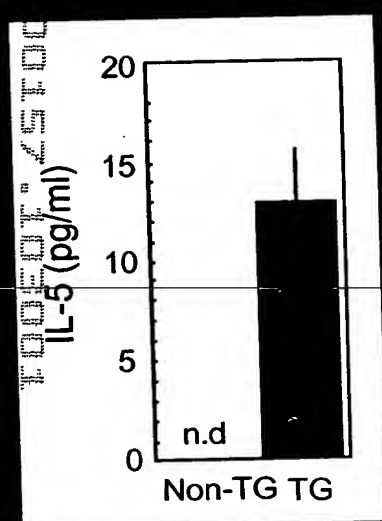


FIGURE 61

Serum IgE and IgG1, but not IgG2a is elevated in mIL-17E transgenics

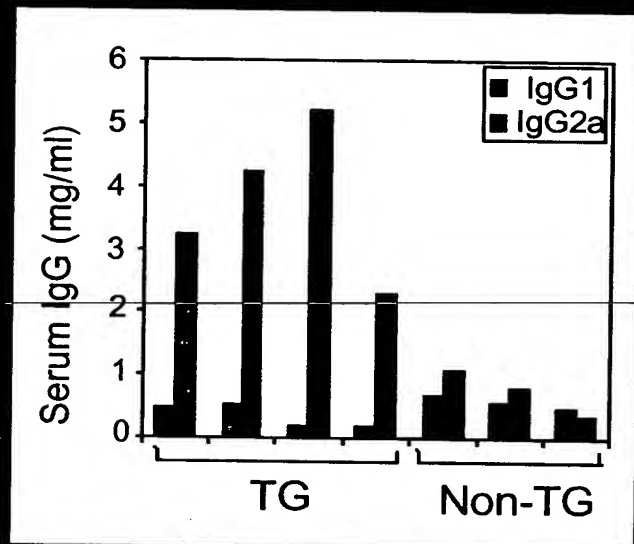
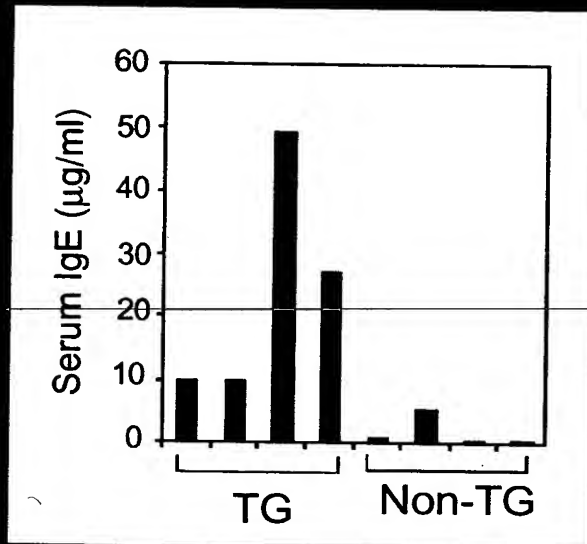


FIGURE 62

# Neutrophilia in mIL-17E transgenics (8 wks, PBMC by FACS)

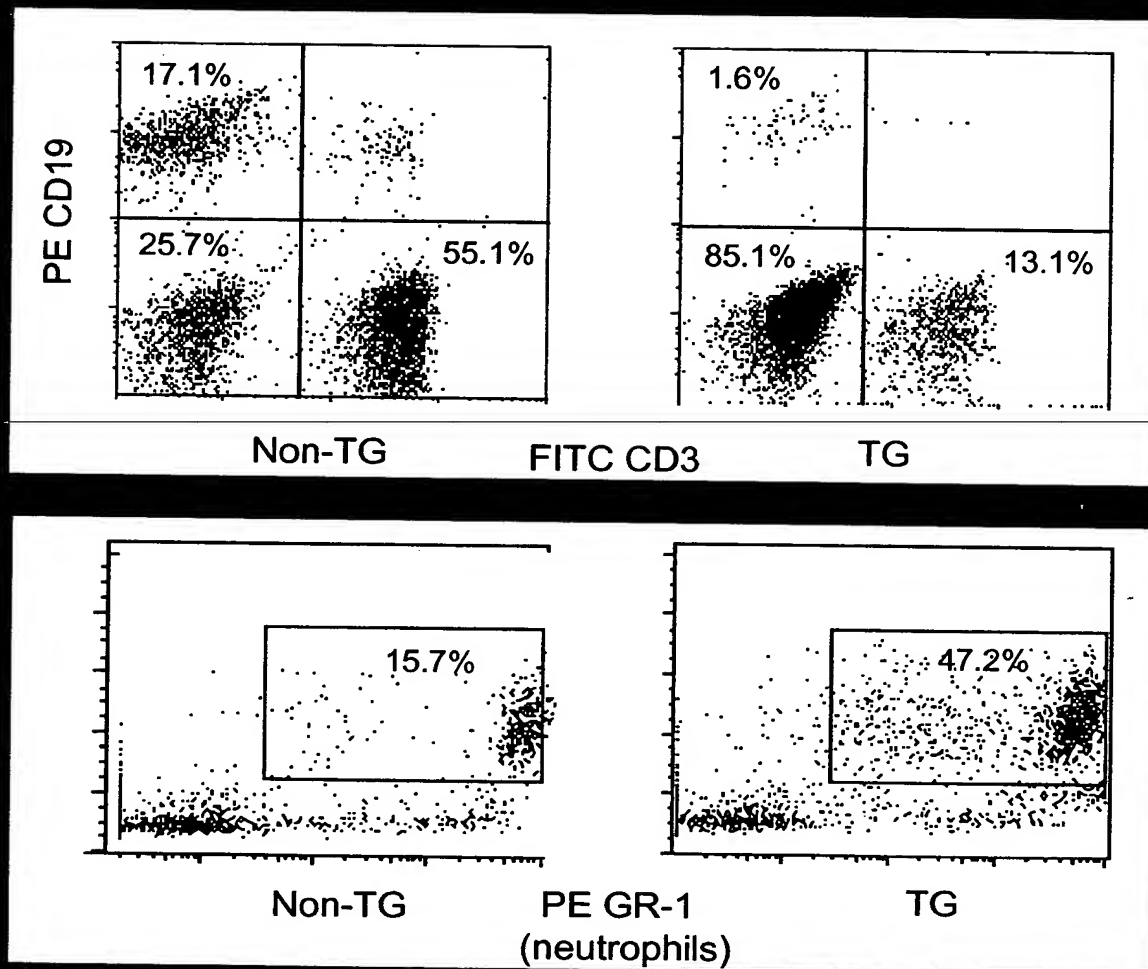


FIGURE 63

# Neutrophilia and eosinophilia in mIL-17E transgenics (hematology)

Absolute cell counts ( $\times 10^6/\text{ml}$ )

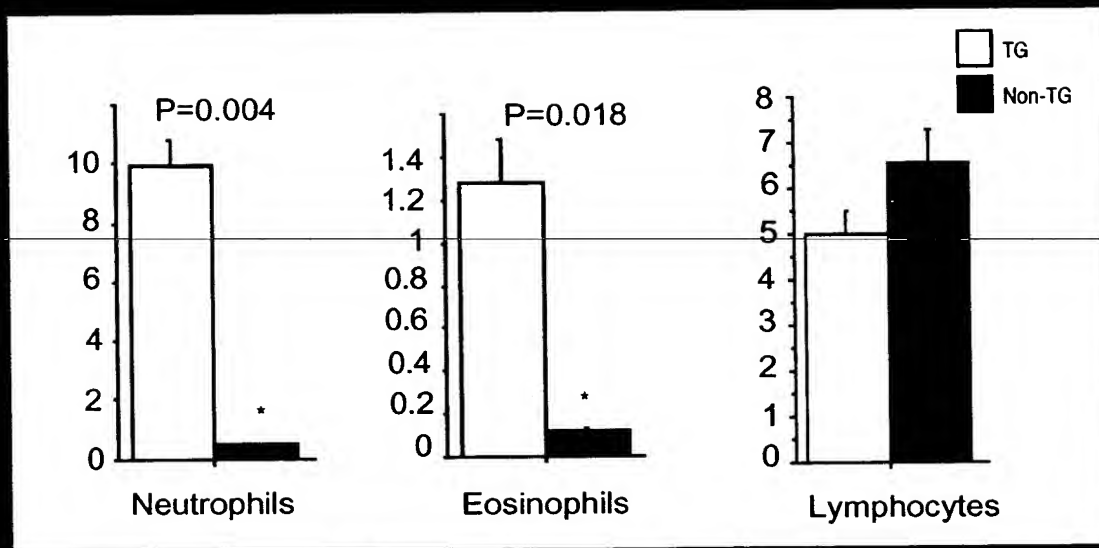


FIGURE 64

G-CSF is elevated  
in mIL-17E transgenics

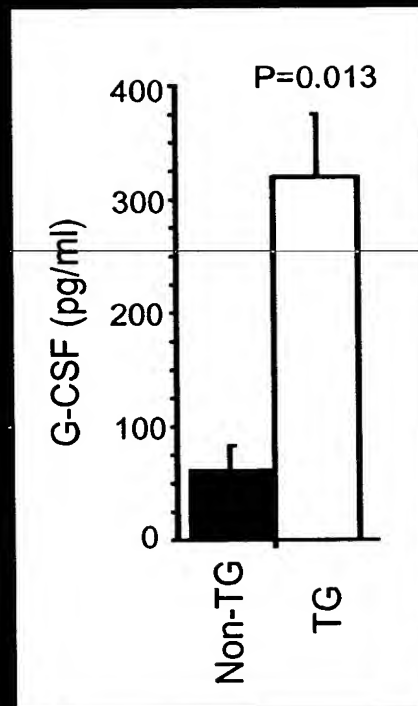




FIGURE 65

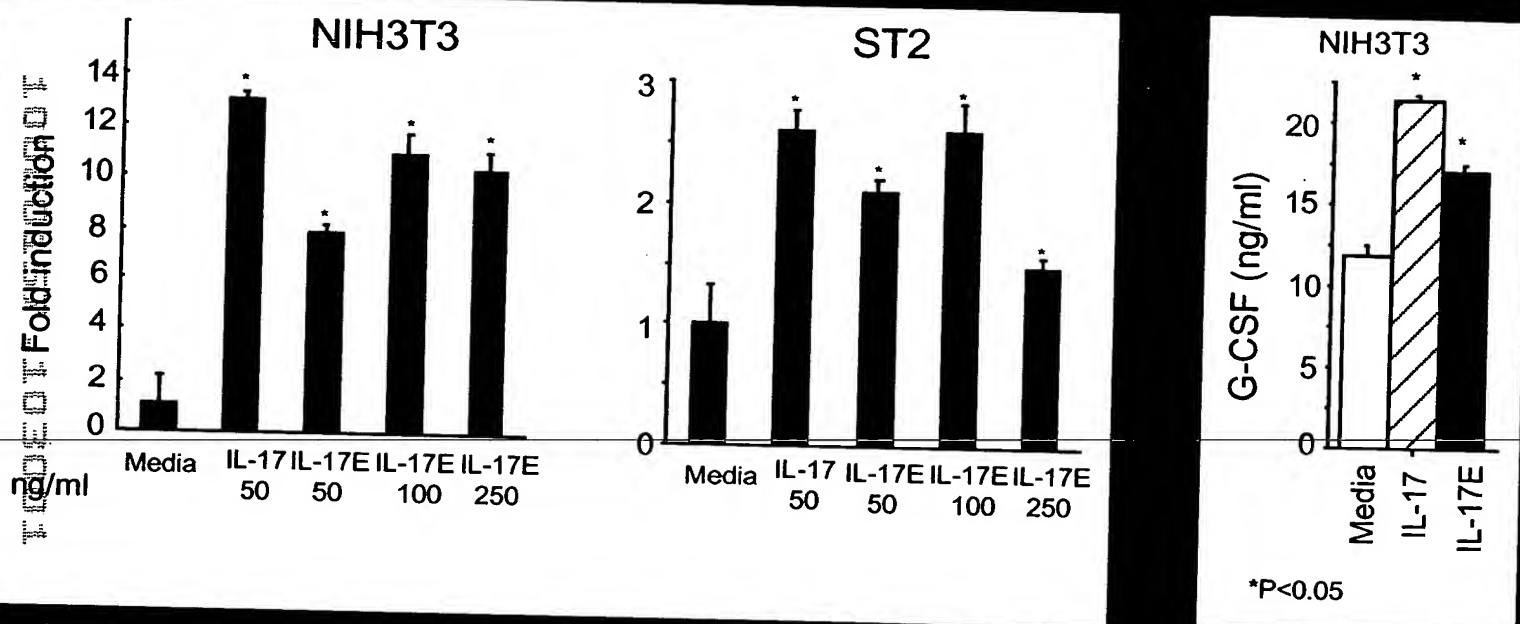
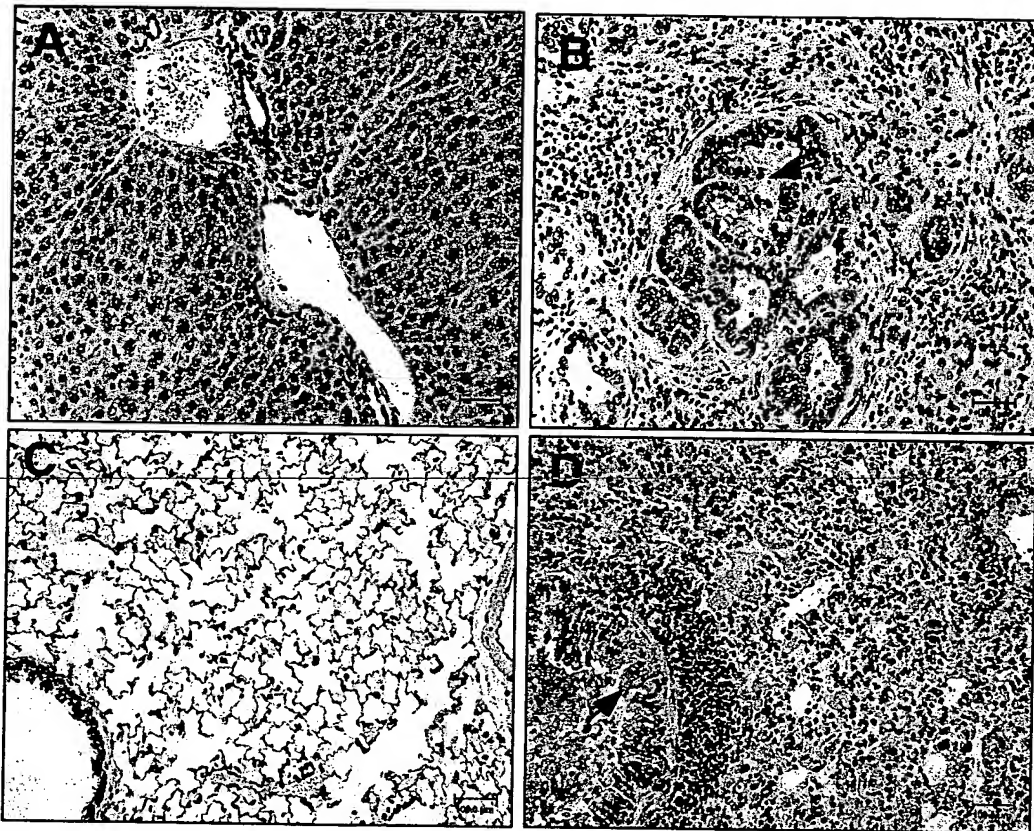


FIGURE 66



10000157-103001